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EDITORIAL

WE MUST LEAD

LESLIE E. DAUGHERTY, M.D.

Today we are in the midst of times characterized by intense, ceaseless struggles by individuals, groups, races and nations for positions of power and influence. In these struggles the ideals of medicine are involved, not as the primary issue, but secondarily in a program of socialized health and welfare. Just what part medicine is to play in guiding its aspect of the program, and whether that part will be to the good or detriment of mankind, will depend upon whether we are motivated only by ego and desire for power or by a real wish to help. These programs should be guided so they will result in a minimal loss of the rights of the individual and the maximum use of the facilities of organized society and government.

Many people say that the movement toward guaranteed medical care and hospitalization for all citizens has gone so far that it will not be turned back. The problem facing us is how to prevent this movement from destroying the doctor-patient relationship, which is built on moral and spiritual values. How well we succeed will depend largely on our own behavior. We will go further by looking for our own errors and respecting our opponents' strengths.

We should realize that some of our legislators look on these medical socialistic welfare programs as being noble in purpose. We are faced, as always, with the fact that the laws of our land are created in the minds of men. It is not always possible to influence the thinking or the actions of a man after he is elected to office. He is aware of who influenced his election. He has to accept his obligations as a representative of the group who elected him, even though he sometimes votes against his own conviction.

Most of us in our profession have been privileged to grow up in religious homes and to have had the advantages of good secondary and higher education. The spiritual, moral and ethical training received during our medical education and growing out of our contact with human beings during times of distress is an added educational experience. No group has a better background for leadership. No group should be more aware of the need for that leadership.

Many changes have occurred in the health programs of our country. Whether these

changes are good or bad, they have occurred, and medicine must furnish the leadership to see that the doctor-patient relationship is not disturbed and that better health programs are available to all.

If medicine takes this leadership in an effort to save for the United States a proud and dedicated profession, we shall be confronted in some areas with the necessity for an occasional change of mind. We shall have to discipline ourselves and learn to cope with difficult situations. We shall need to become astute politicians and statesmen. We shall have to learn the art of compromise without straddling a fence and without losing sight of our goal.

LONDON

$925 Round Trip*

The Faculty is planning a European tour for its members, immediate family, and friends during the summer of 1960. The tour (as a group) PARIS is tentatively scheduled COPENHAGEN to depart on July 15 by JET (Boeing 707) returning (individually) when you so desire, within the three week limitation or beyond it.

A Joint Clinical Conference is planned with the British Medical Association for July 18. After the clinical conference, you, your family, MOSCOW and friends are free to travel as you choose. Please indicate your interest in the ROME tour by mailing the form appearing in the Executive Secretary's newsletter.

* This cost represents 22 days of European holidays—all inclusive expenses—first-class hotels, meals, sightseeing tours, and transportation. The current economy rate—New York-London—is $502.00.

Heart Association of Maryland

Articles in this special issue have been prepared by members of the Heart Association of Maryland. We acknowledge the efforts of Charles F. O'Donnell, M.D., Richard S. Ross, M.D., and Leonard Scherlis, M.D. in gathering and editing material for this issue.

THE HEART ASSOCIATION AND THE PRACTICING PHYSICIAN

LEE S. BOWERS*

The Heart Association is a voluntary nongovernmental association of citizens who share the common goal of controlling heart disease. The Heart Association receives financial support through voluntary contributions and spends these funds in ways decided by its own governing body for medical research, professional education, public education and services to the community. To fulfill its purpose, the Heart Association is constantly exploring new ways to meet recognized needs in the cardiovascular field.

The Heart Association of Maryland is affiliated with the American Heart Association. There are nine Maryland county heart chapters affiliated with the Heart Association of Maryland. This somewhat parallels the relationships between the Medical and Chirurgical Faculty of Maryland, the county medical societies and the American Medical Association. Every physician in the state is serviced by a Heart Association chapter.

Originally an all medical scientific body, the Association expanded in 1948 to become a cooperative endeavor between lay persons and the medical profession. In Maryland there are more than 1200 physicians and nonphysicians sharing membership in the American Heart Association through the Maryland affiliate and its chapters.

The relationship of physician members to the Association is best brought out through examination of the reasons why physicians have joined the Association. A report by the House of Delegates of the American Medical Association in 1957 points out that physician members serve in one or more of four different ways. A physician may be a member and active in the program because of his professional interest in heart disease control, or he may be acting as a private citizen interested in his community regardless of his profession. On the other hand, he may be serving because he was called upon as a physician in ways suggested by his specific professional interest or because he is a representative of another professional group, such as a medical society. Whatever his affiliation, he becomes part of a team effort in an all-out fight against heart disease.

Like the medical society, the Heart Association adheres to accepted moral and ethical principles, which include the assumption of obligations to the medical profession, especially in the formulation of policies regarding medical care, preventive medicine and all matters involving physicians and their relationships to the agency and to its clients. This includes cooperative program planning and mutual exchange of information with the medical society.

The first phase of the attack on heart disease is research. The Heart Association does not itself engage in research but supports investigators through fellowships and grants-in-aid. In general, support is directed toward investigators but not to the exclusion of projects themselves. Over the past ten years, the American Heart Association and its affiliates have channeled 40 million dollars into research.

Research must ultimately be applied to patient care to be of useful value. It is the purpose of the

* Director of education, Heart Association of Maryland.

Heart Association's intensive professional education program to assist in getting the latest information gained through research to the practicing physician. This program is reaching physicians through its four professional journals, scientific exhibits, postgraduate courses and seminars, as well as special mailings. The association also maintains a physician's teaching aid service which loans films, slides and special equipment, and provides speakers for medical groups. The association, through its Professional Education Committee, is interested in all ways of helping physicians obtain the latest knowledge in the heart field that they might apply it in their practices.

The community services of the association are of valuable aid in the rehabilitation of patients with cardiovascular disease. These services, which are available only through physicians, have been established by physicians to meet specific needs of heart patients in Maryland. The entire service program is administered under policies established by the medical profession. Included are a program for the evaluation of employment capacity, rheumatic fever control programs, occupational therapy, hospital equipment loan, information-referral services and recreational programs for cardiac children. The Community Services Committee is charged with the continual evaluation of facilities and services for the care and rehabilitation of persons with cardiovascular diseases.

In addition to providing these more direct services, the Heart Association is aiding the physician through its public education program, aimed at teaching the public its role in heart disease control. Education is especially important in certain phases of heart disease control, such as the prevention of rheumatic heart disease, because the public can actively participate in a control program.

In other forms of cardiovascular disease which are presently less preventable, the association is enlightening the public in an attempt to relieve unnecessary fears and misconceptions that stand in the way of detection or therapy, and to motivate persons to see their physicians when necessary. The patient education service makes patient education materials available to physicians for use with their patients. These materials are designed to help the doctor gain the understanding of his patient as to the nature of the disease and the reasons for his recommendations.

Dr. Paul Dudley White recently commented, "We have made more progress in the fight against heart disease in the last ten years than had been made in all the centuries before." With the continued support of all physicians, the Heart Association will continue to grow, and the advances already made in the fight against cardiovascular diseases in the last ten years will be dwarfed by the discoveries of the next decade.

Summary

In the Heart Association, a private agency supported by voluntary contributions, the medical profession and the lay public are joined in a team to fight cardiovascular disease. In Maryland there is a state association affiliated with the American Heart Association, and nine chapters affiliated with the State Association. There is a statewide membership of 1200 physicians and nonphysicians.

The Heart Association's activities, which are governed by accepted medical ethics and practices, are built upon a sound research program. Directly adjunct to research there is an intensive professional education program to help keep the physicians informed of the latest discoveries in this field. In addition, the Association is constantly exploring unmet cardiovascular disease needs in Maryland. Specific services are provided to the community through the Association to help meet these needs. Currently there are work evaluation, occupational therapy, recreational therapy for children, equipment loan and other services. Woven throughout the program is a public education effort to enlighten the public as to its role in preventing, detecting and controlling heart disease. The alliance between physicians and lay persons such as is found in this voluntary health agency has been an effective one in tackling the heart disease problem, our number one health hazard.

1140 Mondawmin Concourse
Baltimore 15, Maryland

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Scientific Papers

REMEDIABLE HYPERTENSION

KATHERINE H. BORKOVICH, M.D.*

Our concepts of hypertension have undergone significant changes during the past 50 years. Hypertension is now considered but one manifestation of a systemic disease. Clinically, the course varies from a relatively benign state, in which the only abnormality is elevated blood pressure, to a fulminant process with widespread arteriolar necrosis. In most patients, the diagnosis of primary or essential hypertension is made by exclusion. In about 10 per cent of the cases of hypertension the condition is secondary to a known disease.

Hypertension of recent onset in a patient less than 35 years of age who does not have a family history of hypertension, or the sudden onset of severe or malignant hypertension in an older person should be considered secondary until thorough study has excluded definite causal mechanisms. The mechanisms of secondary hypertension may be grouped as: (1) Renal, (2) Endocrine, (3) Cardiovascular, (4) Neurogenic. Renal hypertension is associated with lesions of the renal artery or with parenchymal disease. Endocrine hypertension is seen in Cushing's syndrome, primary aldosteronism, and pheochromocytoma. The common types of cardiovascular hypertension occur with coarctation of the aorta and with aortic arteriosclerosis. Hypertension associated with bulbar neuropathy in poliomyelitis and acute porphyria is neurogenic. Three of these specific causes of potentially reversible hypertension warrant further discussion, namely unilateral renal disease, pheochromocytoma and primary aldosteronism.

Hypertension Due to Unilateral Renal Disease

The syndrome of hypertension due to unilateral renal disease has caused widespread clinical interest since Goldblatt's classical experiments in 1934 demonstrated that hypertension could be produced in some dogs by reduction in arterial blood flow to one kidney. This hypertension could be eliminated by re-establishment of the normal renal arterial flow or by surgical removal of that ischemic kidney. In 1937, Dr. Butler reported a patient who had undergone nephrectomy for unilateral pyelonephritis, with recovery from the hypertension. In 1938, Dr. C. Holmes Boyd and Dr. Lloyd Lewis reported a case of a 31 year old man who had had abdominal pain for 11 weeks and hypertension for three weeks due to thrombosis of the right renal artery. This patient still has a normal blood pressure, now 20 years after his nephrectomy. During these past two decades, there were well documented cases which showed that removal of an ischemic kidney or the re-establishment of an adequate renal blood flow was followed by disappearance of the hypertension.

A review of the literature concerning patients whose unilateral renal disease was due to occlusive disease of the renal arteries showed that leukocytosis, polyuria, albuminuria and impairment of urinary concentrating ability may all be reversible. When unilateral renal disease produces hypertension, the clinical course is an accelerated one and the hypertension is of short duration. Retinopathy and headaches are common and the diastolic pressures are high. A series of 35 patients collected by Dr. Merrill and associates at Peter Bent Brigham Hospital revealed an unexpected preponderance of male patients, namely 28 out of 35, a fact that had not previously been noted. The reason for this predominance in males is unknown. Polyuria may be an important clinical symptom in the bedside diagnosis of unilateral renal disease. The polyuria may be due to the pharmacological activity of renin or hypertensin since physiological studies have demonstrated that renin and hypertensin cause a decrease in the tubular reabsorption of water,

* Assistant professor of medicine, The Johns Hopkins University School of Medicine.

sodium, and of chloride in rabbits; and polyuria and polydipsia have been produced in rats by renin and hypertensin. Very high renin concentrations were demonstrated in the renal venous blood of Dr. Merrill's patient, who had unilateral renal disease and who made a complete recovery following nephrectomy. Albuminuria has also been present in a high proportion of such patients, one series reporting 28 out of 30 cases. One may speculate about the role of renin in the production of this proteinuria since high levels of circulating renin have been shown to effect massive proteinuria in the laboratory animal, presumably by increasing glomerular permeability.

One of the classic criteria of unilateral occlusive disease of the kidney has been that the involved kidney, in contrast to the normal one, is unable to excrete intravenously administered dye and that retrograde studies reveal a normal kidney on both sides. In Dr. Merrill's case and also in 10 out of 26 cases that he reviewed, intravenous pyelography did partially visualize the ischemic kidney. This same fact also has been recently emphasized by the workers from the Cleveland Clinic, namely Drs. Dustan and Poutasse. One of the requisites for the production of hypertension in unilateral renal disease is that the occlusion is not complete and that some blood does flow to the kidney. In the reported cases, a portion of the affected kidney has been supplied by one or more unoccluded branches of the renal artery or by an aberrant renal artery arising independently from the aorta. Absolute diagnostic findings for the demonstration of arterial occlusion, then, need not include the nonvisualization of the affected kidney by the intravenous pyelogram. In four of the 15 patients reported by Dr. John Eager Howard from the Johns Hopkins Hospital, intravenous pyelograms indicated normal kidney size and calyceal outlines and no impairment of function of either kidney by usual tests. More frequently, however, in his series the diseased kidney was 1 to 3 cm. smaller than the normal one. Aortograms were done in only three of these 15 patients, and in each instance unilateral renal arterial defects were demonstrated. Studies of total renal function usually have indicated adequate reserve, but occasionally significant impairment has been noted. In Dr. Howard's series, two patients had definite evidence of bilateral reduction in renal function, and removal of the functionless kidney alleviated the hypertension without affecting the function in the remaining kidney. A striking instance has been reported by Drs. Imber and Clymer, wherein removal of an ischemic kidney from a patient with severe hypertension, azotemia, albuminuria and hyposthenuria resulted in the return of blood pressure to normal and a disappearance of these renal abnormalities. It appears, then, that deterioration in renal function may be a physiological or pharmacological phenomenon, not necessarily reflecting irreversible organic disease of the intact kidney.

In 1950, Dr. Harvey White reported his observations in dogs, which showed that changes in renal function followed the gradual diminution of the size of one renal artery when the other one was left intact. The urine from each kidney was collected simultaneously, and Dr. White observed that on the ischemic side urine volume was uniformly reduced. The sodium concentration in this same sample was also reduced and often before either inulin or hippurate clearances were measurably altered. Dr. John Eager Howard and his coworkers at the Johns Hopkins Hospital in 1954, reported their observations on hypertension resulting from unilateral renal vascular disease and its relief by nephrectomy in the *Bulletin* of the Johns Hopkins Hospital. Their fourth case in that report was a patient who had severe hypertension, normal intravenous pyelograms and demonstrable constriction of the right main renal artery by aortogram. That patient had simultaneous ureteral catheterizations done, and exactly such differences as Dr. White had described in his dogs were found in the patient; that is, there was a smaller amount of urine obtained from the kidney with the narrowed renal artery, and that urine sample contained a lower sodium concentration when compared with the urine obtained from the opposite kidney. The ischemic kidney was later removed and the patient's blood pressure became normal. Further study of simultaneously collected urine from the two kidneys in hypertensive patients was therefore undertaken, since Dr. Howard and his group felt that the results suggested that such data had value in predicting when disease in one kidney was responsible for hypertension.

In the *Bulletin* of the Johns Hopkins Hospital for June, 1957, Drs. Connor, Berthrong, Thomas and John Eager Howard reported their experience with

a series of 21 patients. Examination of the kidneys from the 15 patients who improved following unilateral nephrectomy disclosed histologic changes thought to be the consequence of reduced blood flow in 14 instances. In those cases showing significant areas of atrophy of the convoluted tubules of the "ischemic" type, the cells of which were nevertheless apparently viable, success in the treatment of hypertension was predicted. The quantity of the altered renal tubules also seemed important, for occasionally islands of this "ischemic" tubular atrophy were present in such trivial amounts as to make it questionable whether the hypertension was a consequence. The "ischemic" atrophy is quite different from the dilated thyroid-like tubules with exceedingly tiny epithelial cells seen in advanced pyelonephritis, particularly if hydronephrosis had been marked. The "ischemic" tubular atrophy was typically seen at the borders of infarcts. It was also commonly found in arteriosclerotic nephritis and was seen in both glomerulonephritis and pyelonephritis, although not as consistently in pyelonephritis as in glomerulonephritis. It was thought that these changes in all of these conditions were probably the result of reduced blood flow, either as a consequence of the associated vascular disease or the scarring of the glomeruli through which most renal tubular blood must flow. In 14 of the 15 cases which were relieved of hypertension, significant areas of this type of tubular atrophy were present and thus made it possible to predict correctly the alleviation of the hypertension following nephrectomy. In the single exception, the removed kidney demonstrated no evidence of convoluted tubular atrophy, although the arteriogram had disclosed a narrowed renal artery. In the six patients who did not improve following nephrectomy, the removed kidney did not show the ischemic type of tubular atrophy in four cases. There are now more than 30 proven cases with such a positive ureteral catheterization test with resultant cure of their hypertension.

A brief discussion of the ureteral catheterization test as performed at the Johns Hopkins Hospital is in order at this time. The technique of the differential sodium excretion test is described in detail in the *Bulletin* of the Johns Hopkins Hospital in June 1957. Dr. Howard has emphasized that careful attention must be paid to all the details of the test. If this is not done this useful test may fall into disrepute for unjustified reasons. The following brief outline should not, therefore, be used as a protocol for the test. Diets of normal sodium content are given for four or five days preceding the test because it has been found that very low sodium concentrations are found in the urine of individuals who have been on extremely sodium-restricted diets. Hydration is assured by the administration of intravenous or oral water. The patient is cystoscoped, and the catheters are passed up the ureters so that the tips of the catheters rest in the pelvis of each kidney about 2–3 cm. above the uretero-pelvic junction. When urine flow seems adequate, at least 1 to 2 ml. per minute from each kidney, the cystoscope is removed and a third catheter is inserted into the bladder. Each ureteral catheter is allowed to drain for a few minutes and this urine discarded. The bladder is then completely emptied with the aid of manual suprapubic compression. Immediately afterward, chemically clean Erlenmeyer flasks are placed under each of the three catheters and the collections are begun. As soon as 50 ml. of urine is obtained from one kidney (and this usually requires 20 to 40 minutes in a well hydrated patient), the bladder is emptied again to determine how much, if any, urine has leaked around the ureteral catheters, thus completing the first collection period. It is preferable to obtain more than one collection period, since the reliability of the test is considered to be increased if the findings in each period are consistent. On occasions, differential phenolsulfonphthalein tests are also carried out in some of the patients. If the patient has had a history of urinary tract infection, an antibiotic is given prophylactically for a few days following the cystoscopy.

Each urine specimen is measured and if the sample contains blood, hematocrit determinations are carried out to make possible correction for serum electrolytes, which presumably enter the urine with the blood. Urine sodium and chloride concentrations are regularly determined and, on occasions, potassium, calcium and phosphorus.

One should not attempt to interpret any test in which only 1–2 ml. of urine is obtained from one kidney since errors incident to such evaluation are far too great for diagnostic security. It is probably unwise to try to interpret a test when the sodium concentrations are less than 10 meq/l from both kidneys, since differences of 3 to 5 meq/l between

the two sides may be quite significant at this low value. There is obviously less likelihood for false interpretation if the urine sodium concentration from one kidney is in a higher range. The degree of variation in water and sodium output which is significant has not been defined. Dr. Howard's experience so far has shown that patients with the smallest differences in the urine from the two kidneys who had a beneficial result from unilateral nephrectomy showed at least a 60 per cent reduction in urine volume and a 15 per cent lowering of sodium concentration in the same urine. Dr. White observed that any narrowing of one renal artery which produced a detectable reduction in arterial flow always resulted in at least a 50 per cent decrease in urine flow from that kidney. With increasing reduction in renal arterial flow, urine volume was lowered even more from that kidney and the sodium concentration in this urine was likewise decreased. Therefore, it is currently believed that anything less than a 50 per cent reduction in urine volume from one kidney in a simultaneous catheterization study is probably not indicative of unilateral ischemia, even though urine sodium concentration may be reduced on this side. This experimental observation is supported by the result of catheterization studies in one of Dr. Howard's severely hypertensive patients who had a consistent 25 to 30 per cent lowering of urine volume from one kidney with a 10 to 20 per cent lesser sodium concentration in this urine when compared with that obtained simultaneously from the other side. Aortogram had revealed a normal renal arterial system. This kidney was later removed and the hypertension remained unaffected. Microscopic examination of the kidney revealed no abnormality.

Dr. Eugene F. Poutasse, of the Cleveland Clinic Foundation, reported at the 54th Annual Meeting of the American Urological Association this year that renal angiography revealed a surprisingly high incidence of occlusive disease of the renal arteries in selected hypertensive patients and that occlusion surpassed other known causes of secondary hypertension at the Cleveland Clinic as a cause of potentially remediable hypertension. Before 1950 no hypertensive patient at the Clinic was suspected of having a renal arterial lesion, and from 1950 to 1954 aortography was used to demonstrate the blood supply in various uropathies and only occasionally in a hypertensive patient. Aortography was then used extensively in hypertensive patients beginning in January 1955, and 87 of 337 such patients examined through March 1959, were found to have occlusive disease of one or both renal arteries. This brought the number of cases discovered by this technique at the Clinic to 93. The occlusive lesion was considered to be the primary cause in the majority of these patients. The arterial lesions were found to be unilateral in 71 patients and bilateral in 22. During this same period only six patients were found to have pheochromocytoma, indicating the relative frequency of these two potentially curable forms of secondary hypertension.

Primary Aldosteronism

Until October 1954 when Dr. Jerome W. Conn, of Ann Arbor, Michigan, first described a new clinical syndrome which he called primary aldosteronism, no syndrome in man primarily due to an excess of mineral corticoids, aldosterone in particular, had been described. The clinical features of his case consisted of intermittent tetany, paresthesia, periodic severe muscular weakness and paralysis, polyuria and polydipsia, and hypertension not accompanied by edema. The laboratory findings were characterized by hypokalemia, hypernatremia, alkalosis, excessive excretion of sodium-retaining corticoids in the urine, normal excretion of 17-ketosteroids and 17-hydroxycorticoids, and alkaline urine with a low specific gravity. The renal tubular defect in water reabsorption was probably secondary to the chronic hypokalemia. This defect had been reported by Drs. Schwartz and Relman as occurring in patients who had been depleted of potassium as a result of overuse of laxatives. In 1942, Dr. Richard Follis described cardiac and renal lesions produced in rats by a diet extremely deficient in potassium. Dr. Conn's first case, which was due to a benign adrenal cortical adenoma, revealed diffuse vacuolar changes in the renal tubular epithelium. These vacuoles did not take up fat or glycogen stains and therefore were regarded as hydropic degeneration. In some areas the renal tubular lesions had progressed to necrosis. There were also a few areas of calcification in the renal parenchyma in his renal biopsies. Severe arteriolosclerosis was also noted in all of the sections. It was Dr. Conn's impression that the

major cause of the renal tubular lesion was the chronic hypokalemia. The associated alkalosis, he felt, may have been responsible in part for the renal calcinosis. The severe arteriolar lesion, he felt, was related to the excessive activity of the sodium-retaining steroid.

The relevant laboratory data then in the work-up of a suspected case should consist of the urine, electrocardiogram, serum sodium, potassium, carbon dioxide combining power, chloride, sugar and urea or nonprotein-nitrogen. The sodium and chloride values in sweat and saliva are greatly depressed in these patients while the potassium concentration is high. Determination of the aldosterone content of the urine may be done by the bioassay method, paper chromatography or by isotope dilution techniques. From the standpoint of localization of the tumor, intravenous pyelograms and perhaps tomograms should be done. Presacral or peri-renal air injection examinations are not without hazard, and since more extensive experience with their use in localization of pheochromocytomas has not proven too useful, and at times information gained from such studies has even been misleading, these examinations are not recommended. A transverse upper abdominal exploration should be done. Most of the tumors have been found either in the adrenal cortex or adjacent to it. In at least two reported cases, bilateral cortical hyperplasia was found, and in one of these cases, which was reported from The Netherlands in 1957 by Dr. Van Buchem, the patient was a 17 year old boy who had suffered from polyuria and polydipsia since early childhood but had had no muscle weakness or paralysis. He had severe hypertension with a diastolic level of 150 mm. and grade 4 eye grounds. All of the chemical abnormalities present in this syndrome were present in his case and increased amounts of aldosterone were found in his urine. He had the most interesting electrocardiographic abnormalities. In his case, one adrenal and nine-tenths of the other one were completely removed. It took five weeks before the electrocardiogram became entirely normal. This delayed recovery of the electrocardiogram after potassium repletion had been observed, although less strikingly, by Dr. Schwartz, in patients recovering from potassium deficiency caused by severe diarrhea. The discrepancy between normal serum potassium level and electrocardiographic findings should probably be attributed to the fact that the intracellular, rather than the extracellular, potassium is of primary significance in the etiology of the electrocardiographic changes. In that patient there was also evidence that recovery of the intracellular equilibrium occurred much later than the extracellular restitution. Postoperatively the urine became markedly acid and the alkali reserve fell to 26 volumes per cent from 56 volumes per cent and the blood pH changed from 7.44 to 7.29.

At the fourth Pan American Congress of Endocrinology last year, Dr. Conn reported that of the 50 cases he had reviewed, he observed that about 85 per cent of them were caused by a single benign adrenocortical adenoma which measured ½ to 8 cm. in diameter and weighed 1 to 36 grams. In three of these cases a carcinoma was found. Since already 50 reported cases have appeared in the literature in this short period of time since Dr. Conn described his original case in October, 1954, it is important that we be aware of this syndrome and consider it in all patients who have hypertension, but in particular in patients who in the presence of adequate renal excretory function excrete an alkaline urine and show loss of urinary concentrating power. The clinical story and electrocardiogram in all likelihood will be excellent screening methods for this disorder.

Pheochromocytoma

Pheochromocytoma produces excess epinephrine and norepinephrine in varying amounts and hypertension, either sustained or paroxysmal, with hypermetabolism and disturbed carbohydrate metabolism. Because clinical signs and symptoms may be inconclusive, pharmacological and chemical tests are employed as aids in diagnosis. Since Drs. Pincoffs and Shipley first successfully diagnosed and removed a pheochromocytoma about 30 years ago, well over 100 cases have been recognized and surgically proven to be functioning pheochromocytomas. In the reported series at this time, more than 50 per cent of the patents have had sustained hypertension at least at the time the diagnosis was made. In the patients with paroxysmal hypertension, anxiety, headache, precordial and epigastric distress occurred, and most of the patients also experienced blanching, chiefly of the extremities, palpitation, shortness of breath, nausea or vomiting and profuse sweating.

Differentiation of paroxysmal attacks of hypertension due to pheochromocytoma and severe anxiety attacks in emotionally labile persons is often difficult. However, most of the reported patients with pheochromocytoma have been reported as emotionally stable. Dr. Pincoffs stressed that in his first case. Although the paroxysms of hypertension are occasionally precipitated by anxiety or exertion in these patients, they are more frequently caused by mechanical factors such as pressure over the tumor. Patients with persistent hypertension due to pheochromocytoma and those with paroxysmal hypertension, when seen between attacks, frequently manifest other pharmacological effects of epinephrine which may be important clues to the presence of the tumor. These include profuse sweating and almost continuously so, rapid pulse, low-grade fever, occasionally accompanied with leukocytosis. Some of the patients have had basal metabolic rate elevations greater than plus 15 and some have been treated for hyperthyroidism with no improvement in their symptoms. Others have been treated for diabetes mellitus which then disappeared after surgical removal of the pheochromocytoma.

The most accurate, specific and direct test for a functioning pheochromocytoma is measurement of the catecholamines, norepinephrine or epinephrine (or both) in urine or blood. High levels of catecholamines can only be detected if there is a continuous secretion of the hormones as in patients with sustained clinical symptoms or if the samples are obtained when attacks occur in the paroxysmal type or are provoked by histamine or mecholyl. Chemical tests for pressor amines may be unreliable after the administration of chlorpromazine, tetracycline and vasoconstrictor drugs and in patients who are uremic or jaundiced. Lymphoblastoma produces increased amounts of catecholamines. Bananas produce markedly elevated conjugated catecholamines in the urine. The question therefore arises whether other foodstuffs may contain these same amines. Collecting the urine on a banana free diet or by determining the free rather than total catechol amines may eliminate this source of error.

A patient was reported by Dr. George Thorn, in August of 1957, in whom the measurement of blood levels at short intervals after the stimulation produced by histamine confirmed the clinical diagnosis after normal urinary levels had previously been reported in spite of hypertensive attacks. Dr. Thorn's case demonstrated that increased blood levels can also be easily missed. During a first positive histamine test, which produced a clinically typical attack, a blood specimen obtained two and one-half minutes after injection of histamine contained normal amounts of epinephrine and only minimally increased amounts of norepinephrine. However, blood samples obtained two, four and ten minutes after histamine injection during a second histamine test showed the four-minute specimen to contain definitely increased amounts of epinephrine and norepinephrine, whereas the two-minute and ten-minute samples showed only slightly increased and normal levels respectively. These findings agree with the observations of Drs. Garcia, Hunzinger, Ritzel and Staub, who observed during infusion studies of 3 to 20 micrograms of norepinephrine per minute that catechol amine blood levels did not rise for the first one to three minutes during the infusion and returned to normal one to four minutes after cessation of the infusion. It is therefore apparent that blood specimens can be drawn too early or too late after the injection of histamine and that increased catechol amine levels can thereby be missed. Studies with pressor amine infusion in healthy human subjects by Drs. von Euler, Luft, Goldenberg and Thorn and his workers have shown that only 1 to 5 per cent of the injected norepinephrine or epinephrine can be recovered in the urine. Undoubtedly, this explains why normal urinary catecholamine excretions may be found in patients with few paroxysms and those excreting rather small amounts of hormones. This seems even more likely if one considers the broad range, varying from 40 to 100 micrograms, of catechol amines excreted daily in healthy persons.

Pharmacological tests which are used are of two kinds. One is designed to stimulate the discharge of pressor compounds from the tumor and thus to reproduce an attack. The second kind is designed to lower the blood pressure by competitive inhibition of the pressor compounds secreted by the tumor. Precautions are necessary with all these tests. Sedatives and rauwolfia may produce falsely positive results with regitine, whereas antihypertensive drugs may produce falsely negative results. Sedatives and narcotics should be withheld for at least 48 hours

prior to the performance of such tests and antihypertensive drugs for at least a week or ten days and perhaps, in the case of the rauwolfia compounds, for a month, since it has been shown that the rauwolfia effect persists in animals for at least a month. A reliable basal blood pressure must be obtained before any of these tests are done. The histamine test should not be done in patients whose basal blood pressure is 170/110 mm. of Hg or greater. The histamine rise should exceed the cold pressor response. Histamine dosage should be that which will not produce severe headache and unpleasant symptoms and the dose of 0.0125 mg. of histamine base is adequate in most patients; in fact, some tumors have fired with smaller doses. The rise in blood pressure should be prompt, occurring within the first minute after the initial drop and not several minutes after the typical histamine headache has occurred. The symptoms produced by the positive histamine test in most patients will completely mimic the spontaneous attack. Benzodioxane or regitine should be available for use if the blood pressure rise is excessive and/or associated with symptoms. The criterion for a positive result is a response in which there is a systolic blood pressure rise of at least 60 mm. of Hg above the pre-injection level and a diastolic rise of 30 mm. of Hg or above occurring promptly within one to four minutes after the injection and with the blood pressure returning to the pre-injection level in five to 15 minutes. At least two false positive histamine tests have been reported, one by Dr. E. Calkins and one by Dr. Chapman. Six false negative histamine tests have been reported. Drugs used to indicate a positive test for pheochromocytoma by inducing a depressor response include at the present time primarily benzodioxane and regitine. Basal blood pressure level again should be in the range of 170/110 mm. Hg. If the values are lower, the depressor response may be so small that adequate interpretation cannot be made. The minimum decrease is 35 mm. systolic of Hg; 25 mm. diastolic of Hg. In the Mayo series, the average depressor response was 76 mm. of Hg systolic and 50 mm. of Hg diastolic. Several false negative responses to benzodioxane have been reported in patients with proven functioning pheochromocytomas. There have also been two false negative responses to regitine. The false positive response to regitine has been reported in from 25 to 40 per cent of the patients tested. Patients in uremia are especially prone to give false positive reactions to regitine. One severe hypertensive reaction to regitine has been reported by Dr. Henry J. L. Marriott, from the Mercy Hospital here in Baltimore. A few reported instances of severe pressor reactions in patients with essential hypertension have resulted from benzodioxane with the production of hypertensive encephalopathy, hemiplegia and cardiac failure.

Tumors secreting primarily norepinephrine are the ones that give the usual clinical symptoms, whereas those secreting epinephrine give the metabolic effects and sustained hypertension. Thirty-three of Dr. von Euler's patients had elevated catechol amine levels despite no symptoms. Two proven cases of pheochromocytomas presented as diabetes mellitus with no hypertension. One of these patients did have excessive sweating. An exploratory laparotomy using the anterior abdominal approach is preferable. Ether or nitrous oxide usually produces a rise in blood pressure if the tumor is present. Spinal anesthesia should not be used since the fall in blood pressure which may occur at the time of removal of the tumor during the operation then cannot be treated effectively, since the natural resources for combating the hypotension would have been altered by the spinal anesthesia. Hypotension otherwise may be controlled with an intravenous drip of norepinephrine or Neo-synephrine.® If the tumor secretes primarily epinephrine, it is usually found near the adrenal gland; whereas if it resembles sympathetic nerves and secretes primarily norepinephrine, it may be found anywhere in the body from the bladder to the neck, including the thorax. The tumors may be multiple. A small number are malignant. In about one-half of the patients who have had functioning pheochromocytomas removed, the blood pressure returns to normal during or shortly after operation; in the other half, in about 20 to 30 days.

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Baltimore 2, Maryland

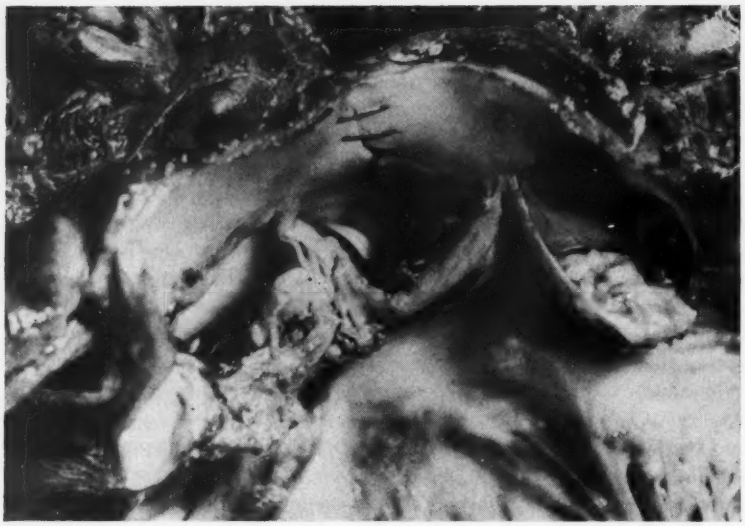

FIG. 1. Autopsy specimen from a patient with aortic stenosis who died of a myocardial infarction after a transaortic valvulotomy (note aortotomy sutures). The aorta and left ventricle have been incised and laid open and the picture was taken from above the valve. The commissure between the right coronary cusp (at left) and the noncoronary cusp is fused and heavy calcium deposits are seen inside the sinuses of Valsalva.

AORTIC STENOSIS

JOHN MICHAEL CRILEY, M.D.*

INTRODUCTION

Recent developments in cardiovascular surgery have focused attention on the common but poorly understood valvular deformity that results in obstruction to outflow of the left ventricle. Aortic stenosis has been a perplexing disease because of its malignant course, resistance to medical management and inaccessibility to surgical correction. On the other hand, some patients with the "classical" signs of aortic stenosis have little or no trouble and often suffer more from cardiac neuroses implanted by their well-meaning physician than from symptoms resulting from their heart disease. The popular concept of the natural history of the disease stems from studies of large numbers of patients by numerous careful investigators, yet there is no unanimity as to prognosis in a given case of aortic valvular stenosis. The development of left heart catheterization has made it possible to study this hemodynamic abnormality accurately, and cardio-pulmonary bypass has made surgical correction feasible.

ANATOMY AND ETIOLOGY

Aortic stenosis results from thickening and fusion of the valve cusps and deposition of calcium, producing narrowing of the orifice and immobility of the leaflets (Fig. 1).

Because the end result is often the same regardless of etiology, figures vary as to the relative incidence of the various etiological types. Congenital deformity is implicated if a characteristic murmur is heard early in childhood or if the condition accompanies other congenital lesions such as coarctation of the aorta. Subaortic stenosis was thought to be invariably congenital, but recently Brock (1) has described acquired diffuse hypertrophy of the subvalvular portion of the ventricle as a complication of systemic hypertension which is quite different from the fibrous ring seen in the congenital variety. Rheumatic disease is implied when there is a history of acute rheumatic fever or evidence of organic mitral valvular disease. Nonrheumatic acquired aortic stenosis has been lumped under the terms "sclerotic" or "calcific." These categories probably contain many patients with unrecognized congenital and rheumatic heart disease, as well as patients with a form of arteriosclerosis affecting the aortic valve. It has been stated that syphilitic aortitis cannot produce aortic stenosis, and there are probably few exceptions to this statement.

PHYSIOLOGICAL ALTERATIONS

When stricture of the aortic valve orifice becomes critical—approximately one-fourth of normal area (2)—the left ventricle must increase ejection pressure in order to maintain adequate arterial pressure and cardiac output. The left ventricular myocardium becomes thickened and literally outgrows its coronary arterial supply. Eventually the muscle is unable

* Departments of Medicine and Surgery, The Johns Hopkins Hospital.

to bear the excess burden, the cardiac output falls, and left heart failure ensues. Arrhythmias are common, and the resultant inefficient cardiac contractions often cause acute diminution of cardiac output (3) leading to syncope or death. Angina pectoris and myocardial infarction often result from inadequate blood supply to the overworked muscle.

Clinical Findings

The physiological changes are manifested in the physical findings of a slow rising, narrow pulse, diminished or absent visible carotid pulsations, forceful left ventricular impulse, cardiomegaly (often only slight), basilar thrill and harsh systolic murmur transmitted to the carotid vessels, and diminution or absence of the aortic component of the second sound. Paradoxical splitting of the second sound, caused by delay in left ventricular systolic contraction, is sometimes noted by alert observers. A systolic blood pressure in excess of 150 mm. Hg is somewhat against significant aortic stenosis.

The electrocardiogram often demonstrates left axis or vertical axis, delayed intrinsicoid deflection over the left ventricle, left ventricular hypertrophy, and inverted T waves in the standard and left ventricular leads. Chest x-rays and fluoroscopy reveal a normal to slightly increased cardio-thoracic ratio, left ventricular enlargement, post-stenotic dilatation of the aorta, and calcification of the aortic valve. The latter finding is seen in almost every case of adult aortic stenosis if careful and specific roentgenography is employed.

The phonocardiogram reaffirms the auscultatory findings noted above. By the oscillographic technique the murmur is "diamond-shaped"; that is, crescendo-decrescendo, beginning shortly after the first sound and ending before the aortic second sound. An ejection click is often seen to initiate the murmur and paradoxical splitting can be demonstrated.

Symptomatology

Many patients are noted to have the classical physical findings of aortic stenosis and have no symptoms whatsoever. This situation often obtains in children and young adults who are discovered to have the condition on school or pre-induction physical examinations. Angina, syncope, and symptoms of left-sided heart failure occur later in the course of the disease, but all of these symptoms can be simulated by coronary artery disease without any significant aortic stenosis. It is important to make this distinction, since surgical therapy directed at aortic stenosis in the latter instance would be useless and possibly disastrous.

Clinical Course

Although many articles (4, 5) have been written on the subject of prognosis, there is little agreement among investigators. The reason for this discrepancy is the lack of precise information regarding the natural history of aortic stenosis. In the past it was necessary to attempt to correlate signs and symptoms with prognosis since it was not possible to measure the actual hemodynamic impairment. The symptoms of aortic stenosis can be produced by coronary artery disease (6) and hemodynamic impairment and symptomatology need not be correlated; therefore it was virtually impossible to gather meaningful data.

Estimates for life expectancy in asymptomatic aortic stenosis range from 10 or 20 years to a normal lifetime. In a series of patients with aortic stenosis followed at The Johns Hopkins Hospital (7), patients developing angina pectoris died within an average of three years, with a range from three months to nine years. Orthopnea, dyspnea, or edema lead to death in about one year, with a range from four days to three years. Syncope can cause death with the first or any subsequent attack. At this hospital, the average duration of life after the first syncopal attack was two years, with a range of one to four years. The presence of all three symptom complexes, *when they are due to aortic stenosis*, indicates a life expectancy of only a few months.

Special Studies

The recent application of cardiac catheterization techniques to the left side of the heart have made it possible to approach an objective evaluation of the above physiological changes (8, 9, 10). The left ventricle can be catheterized through the left atrium, retrograde via the peripheral arteries and aorta, or directly punctured percutaneously with a no. 20 or no. 22 needle at the apex. The latter route is somewhat preferable because of the directness of the approach and the higher yield of satisfactory studies. However, the other routes possess certain advantages, such as the ability to study left atrial hemodynamics simultaneously or consecutively in the approach through the left atrium and to leave a catheter in place longer in either catheterization method.

Surprisingly, left ventricular puncture has been quite innocuous, with only one reported mortality

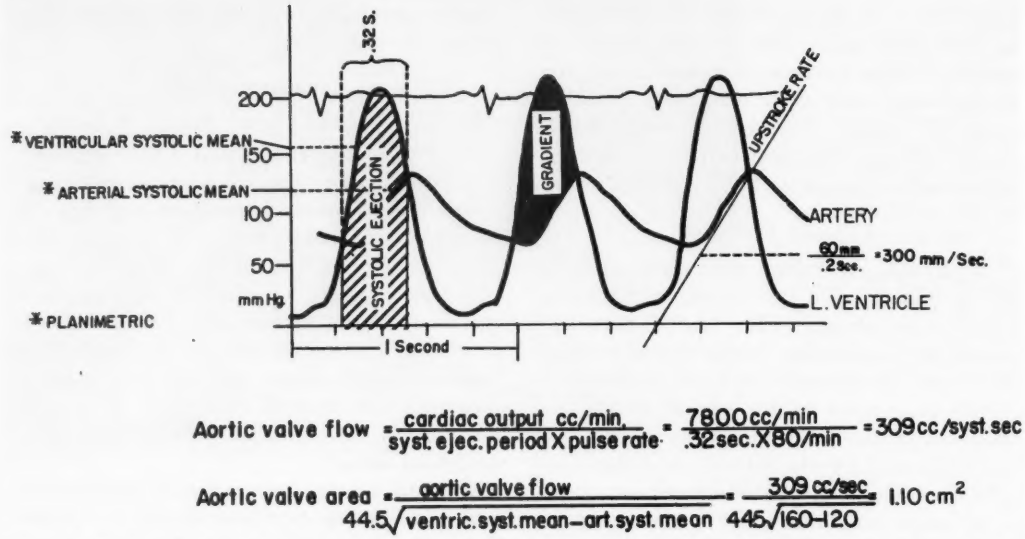

FIG. 2. Tracing of left ventricular and brachial artery pressure curves from a patient with aortic stenosis. The actual values for pressure and flow are used in the Gorlin formulas at the bottom and a valve area of 1.1 cm.² was calculated. The values for mean systolic pressures were obtained with a compensating polar planimeter.

(11) in thousands of successful studies. The success of the technique is a reflection of the extreme caution of the operators. Many of these studies are done in the operating room and virtually all are done with a cardiac surgeon in attendance and equipment at hand for emergency thoracotomy and electrical defibrillation. Fortunately, the hypertrophied left ventricle has great self-sealing qualities.

The parameters necessary for complete evaluation of aortic stenosis are the left ventricular pressure curve, arterial or aortic pressure curve, and a measurement of cardiac output. From analysis of these factors and application of modified hydraulic formulas, a reasonably accurate estimate of the aortic valve orifice can be obtained. In addition to this ultimate measurement expressed in square centimeters, various ancillary data can be derived which are helpful in estimating other factors such as aortic regurgitation and the degree of myocardial failure.

Pressure Pulse Analysis

The simultaneous or consecutive pressure curves in the left ventricle and a peripheral artery can be measured with transducers and recorded on an appropriate recording instrument, properly calibrated with mercury, and analyzed in the following manner.

Gradient: The sine qua non of aortic stenosis is a left ventricular pressure in excess of the arterial pressure. The presence of this difference, or gradient, is abnormal and its absence rules out hemodynamically significant obstruction (fig. 2). However, the magnitude of this gradient by itself cannot be relied upon to determine the degree of stenosis. This point will become obvious later.

Aortic or peripheral artery curve: The arteriogram in aortic stenosis reveals a slow "upstroke," an early anacrotic notch, and a sustained systole (11) (fig. 3). Although it is hazardous to depend on empirical figures in evaluating upstroke rate, a value of less than 750 mm./second suggests aortic stenosis and a rate of 1000 mm./second or more implies that there is either combined stenosis and regurgitation or no critical stenosis. The presence of a "bisferiens" or double-peaked curve, especially with a rapid upstroke, usually denotes a significant degree of aortic regurgitation and makes aortic valvulotomy inadvisable. Pulsus alternans is often seen in both the arterial and ventricular pressure tracings.

Ventricular curve: In addition to having a high systolic pressure peak, the ventricular curve exhibits a prolonged systolic ejection. This prolonged ejection period is necessary for the ventricle to eject an adequate stroke volume through a restricted orifice. A high pressure (in excess of 10 mm. Hg) at the end of ventricular diastole suggests cardiac failure.

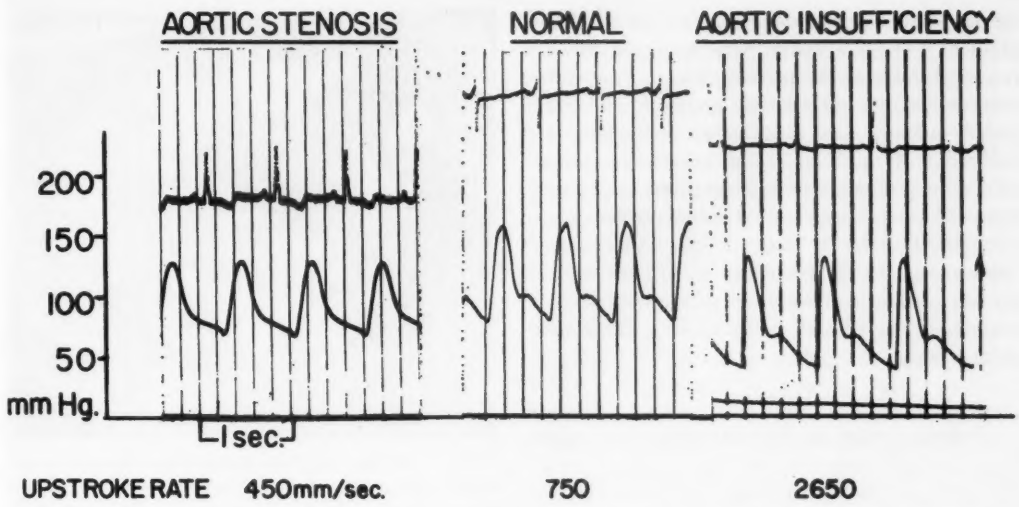

FIG. 3. Arterial tracings from three patients with murmurs of aortic stenosis. The patient whose tracing is shown at left was found to have severe aortic stenosis at operation. No significant gradient was demonstrated across the aortic valve in the other two patients shown. The electrocardiogram is shown at the top of the three records.

Cardiac output measurement: A measurement of cardiac output at the time of pressure measurement is essential if a reliable estimate of aortic stenosis is to be made. This measurement can be made by the Fick principle or with dye dilution curves. The latter technique is preferable because it can be done nearly simultaneously with the pressure measurements. The Fick method is equally accurate, but the necessity of expired gas collection and mixed venous (i.e., pulmonary artery blood) sampling makes it difficult to measure the output at the time of catheterization. Another advantage to the dye method is that gross aortic regurgitation will often be reflected in the contour of the dye curve.

Calculations: The aortic valve flow and area are calculated by the Gorlin formulae (12, 13), which are:

$$\text{Aortic Valve Flow} = \frac{\text{Cardiac Output}}{\text{Systolic Ejection Period} \times \text{Pulse Rate}}$$

$$\text{Aortic Valve Area} = \frac{\text{Aortic Valve Flow}}{44.5\ (\text{gravity constant}) \times \sqrt{\text{Systolic Gradient}}}$$

Perusal of these formulas reveals that the aortic valve flow is directly proportional to cardiac output and inversely proportional to systolic ejection time and heart rate. The larger the flow with a given gradient, the larger the aortic orifice must be. The following table illustrates some hypothetical cases in which cardiac output, valve area, and gradient are varied.

Conditions		Cardiac Output L/Min.	Valve Area cm^2	Gradient mm. Hg	Note
Area constant Output tripled	A B	5 15	1 1	14 125	Same valve area can give small or large gradient depending on output
Same gradient Output doubled	A B	6.7 13.3	0.5 1	100 100	Same gradient can be caused by valve areas with twofold difference in size
Same output Valve area doubled	A B	5 5	0.5 1	75 14	Halving valve area can increase gradient fivefold at same cardiac output

NOTE: A heart rate of 100 and a systolic ejection period of 0.3 second were used in the above calculations.

It can be seen that the gradient is meaningless without knowledge of the other parameters, since a large gradient can be caused by a large cardiac

output and a tight valve can produce a small gradient if the flow is low. Another factor, which is not measurable at the present time, is *forward flow* across the aortic valve during systole when there is mixed stenosis and insufficiency. Obviously the forward flow must equal the net cardiac output plus the regurgitant flow and a gradient can be quite high with a seemingly normal or low cardiac output when insufficiency is present. The cardiologist is often alerted to the possibility of such an inflated gradient when a collapsing pulse and diastolic murmur are noted and the upstroke in the arteriogram is rapid.

Therapy

Medical therapy in the management of severe aortic stenosis can only be supportive. The arrhythmias which acutely lower the cardiac output and frequently produce syncope and death can sometimes be controlled through judicious use of digitalis and quinidine. Digitalis and diuretics in the treatment of congestive failure are, at best, temporarily palliative since this complication is indeed dire and often preterminal. Coronary vasodilators are of questionable value in the treatment of angina and are considered contraindicated by some cardiologists. Certainly rest and maintenance of a nearly basal state can prolong life if the patient is willing to pay this price.

Surgical management offers the only chance of prolonged useful life in severe aortic stenosis and should be given careful consideration in every patient with this condition. The transventricular route employing an expanding valvulotome was the first successful approach and is still being used by many surgeons (14, 15). It has the advantage of short operating time and low mortality rate. The obvious disadvantages are the necessity of puncturing the left ventricle with a large instrument and the lack of visual control. A modification of this procedure is a transaortic approach with a valvulotome. However, the low mortality rate is somewhat counterbalanced by technical failure and the occasional production of severe insufficiency. It has been shown that expansion of the dilator under direct vision in fresh autopsy specimens often fails to alter the valve noticeably, since the cusps are semi-rigid and spring back to their former position immediately after withdrawal of the blades. More recently, a transaortic approach with cardiopulmonary bypass or hypothermia has permitted direct vision of the valve (16, 17, 18).

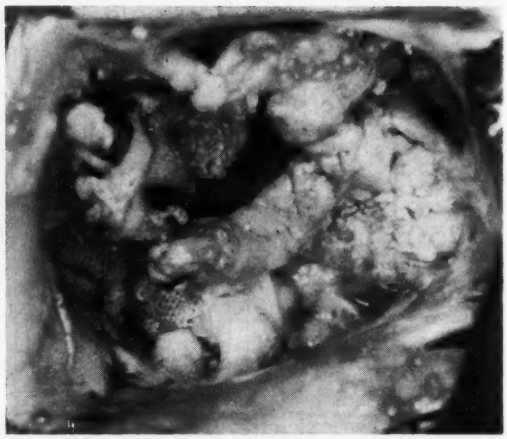

Fig. 4. Autopsy specimen of a postoperative patient with severe calcific aortic stenosis. The picture was taken from above the valve, looking down through the valve orifice. The landmarks are obscured by calcification, and in order to relieve the stenosis an entire cusp was removed and replaced with prosthetic material (7 o'clock in picture).

In many patients the surgeon is able to remove calcium from the valves to restore flexibility, open commissures and effectively restore patency without producing valvular insufficiency. However, the technical problems are considerable. The hypertrophic left ventricle tolerates prolonged anoxia poorly, and a patient with an excellent valvular reconstruction may succumb to a myocardial infarction or diffuse myocardial damage. This problem is now being combated with techniques of coronary perfusion. All too frequently, once exposed, the valve is found to be beyond repair (fig. 4). Occasionally, nearly all the landmarks are obscured by heavy calcification and the only hope is removal of one or more cusps and replacement with prosthetic material. Unfortunately this procedure, at present, is rarely satisfactory. There is no doubt that this type of valve will remain virtually impossible to reconstruct until a satisfactory prosthetic valve is available. Prospects are encouraging for such a valve in the near future.

On the more optimistic side, surgical results have been good and the mortality respectably low in young patients with aortic stenosis treated by open heart surgery (19). The success in children and young adults is due to the lack of heavy calcification and the greater myocardial reserve in these patients. Calcification probably occurs in 80–90 per cent of patients over 35 years of age, but is uncommon under the age of 20. The acquisition of calcium on a

deformed valve is probably related to turbulence and usually takes about 20 years to develop.

Discussion

The physician responsible for a patient with aortic stenosis is in an unenviable position. The choice lies between an uncertain and often fatal natural history and a technically difficult and possibly fatal operation. Although much is still unknown, the available facts suggest a rational approach to the disease which may benefit both patient and physician.

First, it is obvious that much more can be learned about the disease by hemodynamic study of more patients with aortic stenosis. The risk to the patient is low and, if the study is done intelligently, the yield to the physician is high. Without specific data, it will be impossible to state with any certainty that in one patient a given degree of outflow obstruction can be tolerated without surgery, while in another patient angina, syncope, cardiac failure and death will ensue unless surgery is performed. The physical findings are difficult to assess objectively, and all of the symptoms can be produced by coronary artery disease without significant outflow obstruction of the left ventricle.

Second, experience has shown that young people tolerate aortic valvulotomy better than adults. This does not mean that all patients with aortic stenosis of any degree should submit to valvulotomy before their twenty-first birthday, but it would seem highly desirable to measure the degree of stenosis in any young patient, regardless of severity of symptoms, and seriously consider the possibility of surgery if critical stenosis is found.

Third, in patients with advanced aortic stenosis in which heavy calcification is seen on x-ray, closed valvulotomy should be carefully considered. Although there are theoretical advantages to direct vision, practical experience seems to indicate that the surgical mortality is lower when cardio-pulmonary bypass is not employed, and the results in heavily deformed valves are no worse. In other words, there is a chance of partial success and less chance of surgical death. It is entirely conceivable that a successful prosthetic aortic valve is on the horizon and that palliative surgery of this type might prolong life and give patients with severe calcific aortic stenosis a chance at a new valve later.

Summary

Heretofore, little was known about the hemodynamic alterations of aortic stenosis, and little could be done for patients with this condition. It is now possible to study these patients accurately with a minimum of risk, and surgery offers many patients a greater life expectancy. In order to manage a case of aortic stenosis intelligently, the physician should seriously consider left heart catheterization, especially if the patient is symptomatic.

Once the extent of the outflow obstruction has been adequately assessed, the decision regarding surgery should be made. If critical stenosis exists, it is certain that aortic valvulotomy offers the only hope of a long, useful life. Children and young adults tolerate open-heart transaortic valvulotomy reasonably well, and this is probably the procedure of choice. In adults with heavy valvular calcification, closed transaortic or transventricular valvulotomy is the rational approach and offers a prolonged life and the possibility of another attempt once a successful prosthetic valve is developed.

614 North Bond Street
Baltimore 5, Maryland

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IMPORTANT DILEMMAS IN CARDIAC ARRHYTHMIAS

HENRY J. L. MARRIOTT,* M.D. AND LEO SCHAMROTH,** M.B., B.Ch., M.R.C.P.E., F.R.F.P.S.

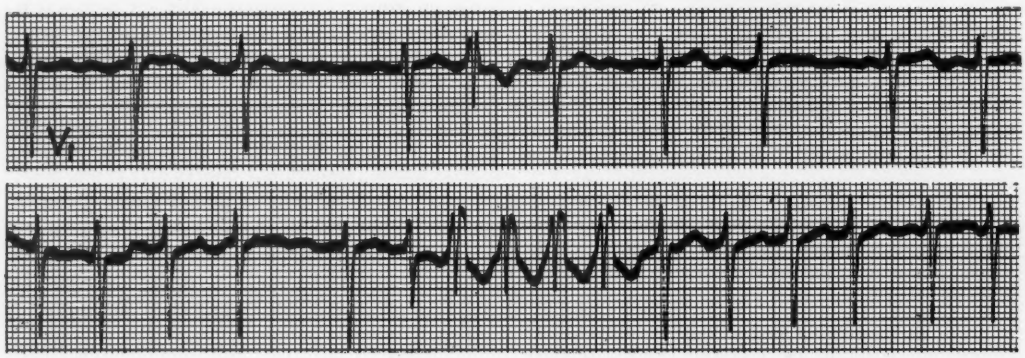

FIG. 1. **Atrial fibrillation with aberrant ventricular conduction.** In the upper strip the fifth beat is bizarre and shows a right bundle branch block pattern; it terminates a short ventricular cycle that is preceded by an unusually long one, and is followed by a pause that makes no attempt at being "compensatory." It therefore has all the hallmarks of ventricular aberration. In the lower strip the sixth beat, terminating a "long-short" sequence, is only slightly aberrant, but the succeeding four rapid beats are markedly so and are similar to the single aberrant beat in the upper strip. This run of aberrant ventricular conduction is characteristically terminated by a slightly longer cycle which is not long enough to consider "compensatory."

To the casual acquaintance of electrocardiography, the arrhythmias seem clear-cut and straightforward. Better acquaintanceship, however, usually reveals that this is far from true; that the arrhythmias may at times present the most baffling and complex of all electrocardiographic problems. We shall here confine our attention to two dysrhythmic mechanisms which frequently lead to misdiagnosis.

VENTRICULAR ABERRATION

The beginner in electrocardiography soon appreciates that the appearances of the ventricular complexes in ectopic ventricular rhythms and bundle-branch blocks are similar. It appears to require a relatively long and intimate apprenticeship, however, before it is recognized that intraventricular block may occur as an isolated phenomenon in early supraventricular beats or in short or long runs in response to a supraventricular tachycardia, so that ectopic ventricular beats or ventricular tachycardia may be closely simulated. This form of abnormal conduction through the ventricles, resulting in bizarre QRS-T patterns that simulate ectopic ventricular rhythms, is known as aberrant ventricular conduction or ventricular aberration (1). Its identification and differentiation from ectopic ventricular mechanisms is important for two reasons: 1—a large number of practitioners, internists and even cardiologists are unaware of the frequency with which such deceptive beats occur; and 2—proper treatment may be jeopardized if the possibility of ventricular aberration is not considered. For example, digitalis is usually the treatment of choice and may be lifesaving in atrial fibrillation with rapid ventricular response, but if the tracing is interspersed with what appear to be more or less frequent ventricular ectopic beats or runs of ventricular tachycardia, the indicated drug may be withheld to the patient's detriment. Figure 1 illustrates atrial fibrillation interrupted in the upper strip by an isolated early beat that looks like a ventricular extrasystole, but which is in all probability an example of ventricular aberration, and in the lower strip complicated by a short run of aberrant ventricular conduction that simulates a short bout of ventricular tachycardia.

It is, of course, common to find the irregularly

* Associate Professor of Medicine, University of Maryland; Chief, Electrocardiograph Department, Mercy Hospital, Baltimore.

** Physician, Baragwanath Hospital and University of Witwatersrand, Johannesburg, South Africa; at present Fellow in Cardiology, Mercy Hospital, Baltimore.

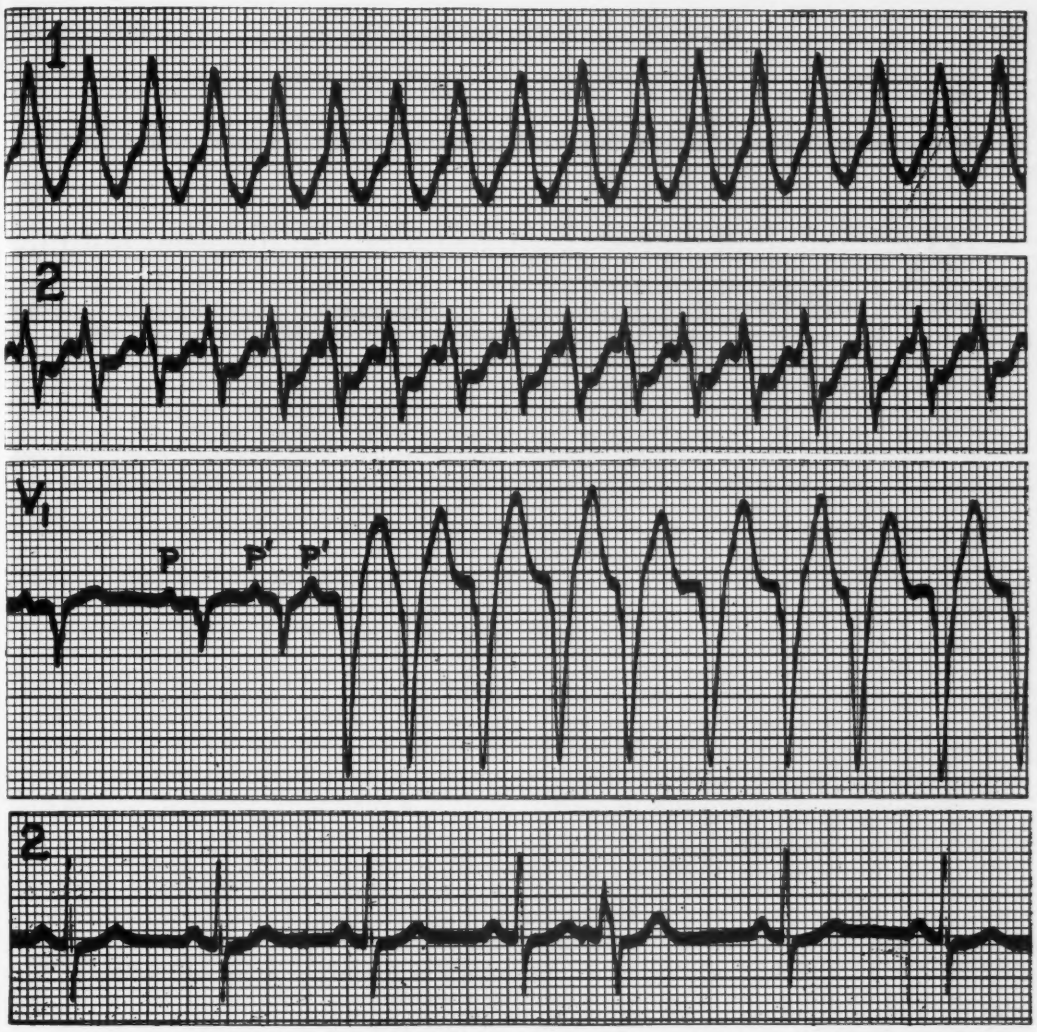

FIG. 2. **Atrial tachycardia with ventricular aberration.** The two uppermost strips show the typical pattern of ventricular tachycardia. In lead V_1, however, a run of apparent ventricular tachycardia is preceded by two rapid ectopic P waves, the first of which is conducted normally while the second is followed by the first beat of aberrant form. Furthermore, in the lower strip of lead 2, a single premature beat, of identical form with the QRS during the tachycardia in the upper strip of lead 2, is clearly preceded by an ectopic P wave and is not followed by a fully compensatory pause. These clues give clear evidence that the tachycardia is of supraventricular origin with concomitant ventricular aberration.

spaced ventricular complexes in atrial fibrillation punctuated by bizarrely widened complexes; these are usually dismissed as ventricular extrasystoles. But it is always important to be aware of the possibility that such beats may not be of ectopic ventricular origin; indeed, there is perhaps an almost 50-50 chance that they represent ventricular aberration. Though the distinction can seldom be made with certainty, there are several points that assist in differentiating.

Ventricular aberration almost always occurs when a relatively short cycle follows a relatively long one. This is because the refractory period of the conducting tissues is proportional to the preceding R-R interval. If, therefore, a prolonged R-R interval with its duly long refractory period is succeeded by a relatively early impulse, conditions are obviously ideal for aberration to occur. Unfortunately, ectopic ventricular beats are also likely to follow after a relatively long ventricular cycle (2) and therefore this long-short sequence is of little or no distinguishing value. On the other hand, ectopic ventricular beats of identical contour tend to show "fixed coupling" to the preceding beat, whereas examples

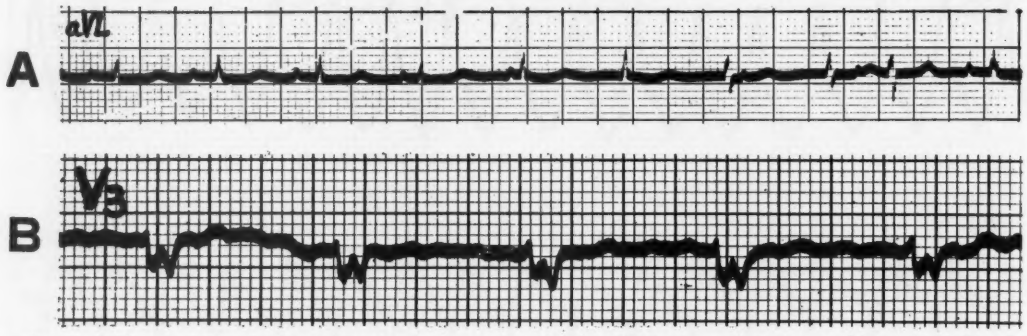

FIG. 3. **A–V dissociation** A. The atria under sinus control are beating slightly slower than the ventricles under A–V nodal control; the P waves therefore "overtake" and "pass" the QRS complexes. When the P wave has emerged sufficiently far beyond the QRS complex, it is conducted to the ventricles—"ventricular capture." The captured beat, incidentally, shows ventricular aberration. B. The ventricular rhythm, despite the presence of atrial fibrillation, is perfectly regular at a rate of 80 per minute.

of ventricular aberration may occur at varying intervals following the preceding beat. Again, ectopic beats tend to be followed by a longer pause—an attempt at a "compensatory" pause—than aberrant beats. Finally, aberrant conduction usually assumes a right bundle-branch block form, whereas ectopic beats are just as likely to show a left as a right branch-block pattern. Even when all these points are taken into consideration, however, the identity of many such beats remains in doubt.

The clinical importance of separating ventricular from supraventricular tachycardias is well appreciated; it does not seem to be well known, however, that this separation cannot always be made by routine electrocardiography. This is because a supraventricular tachycardia is not uncommonly complicated by ventricular aberration, and this combination is almost always impossible to distinguish from ventricular tachycardia in the conventional leads. It is, therefore, worth enumerating the points that may be of differential value. Figure 2 illustrates a case in point—an atrial tachycardia masquerading as ventricular.

First and foremost, bedside examination may be more conclusive than the routine electrocardiogram; thus Schrire and Vogelpoel (3) found that of ten consecutive examples of eventually proven ventricular tachycardia, they could be certain of the diagnosis from the conventional electrocardiogram in only two, whereas they could make the diagnosis in all ten by careful auscultation. If the arrhythmia is a ventricular tachycardia, the first sound at the apex *with the breath held* will almost always vary in intensity and, at the same time, occasional irregular cannon waves in the neck veins may be seen. Both of these phenomena are due to the dissociated activity of the atria which are beating at their own slower rate independent of the rapid ventricles. On the other hand, in a supraventricular tachycardia where the A-V sequence of contraction is undisturbed, the first heart sound should be of constant intensity and the venous rhythm should not vary from cycle to cycle.

In the electrocardiogram, "cherchez le P" is the golden rule. If the tachycardia is occurring in bursts, P waves at the onset of a paroxysm may point to the diagnosis (fig. 2, lead V_1). If no P waves are apparent in any of the routine leads (they are most likely to be visible in V_1), they must be looked for in special leads: CR_1 and S_5[1] should first be tried and if these, too, are found wanting, an esophageal lead should be attempted. A technically satisfactory esophageal lead will almost invariably reveal the P waves and so solve the riddle. Occasional aberration, present in isolated premature supraventricular beats between paroxysms and identical with the ventricular pattern during a paroxysm, may provide the necessary clue (fig. 2, lead 2).

Failure to recognize ventricular aberration may perhaps account for some of the cases of "ventricular" tachycardia that have responded to digitalis; it may also in part explain the statement that ventricular extrasystoles are more likely to be seen in the presence of atrial fibrillation.

A-V Dissociation

A more maltreated dysrhythmia than A-V dissociation cannot be found. The term is applied, not improperly, to all manner of disturbances, momentary or prolonged, in which the actions of atria and

[1] Obtained by attaching precordial electrodes to the two arm wires, placing the negative (right arm) electrode over the manubrium and the other in the fifth right interspace, and recording a bipolar precordial lead with the selector switch at lead I.

ventricles are more or less dissociated and independent. On the other hand, some authors apply the term more specifically, as we are doing, to a certain group of dysrhythmias for which no satisfactory collective term has yet been universally accepted; the prototype of this group is that which has been called interference-dissociation or dissociation with interference (fig. 3A). But as A-V dissociation is also freely and quite legitimately used for complete A-V block by many authorities, confusion between these quite dissimilar arrhythmias frequently arises. The confusion surrounding A-V dissociation is further confounded when high authorities choose to use the term interference in diametrically opposed senses. Terminology, however, is not our concern here; it has been fully and frankly discussed previously (4).

We are mainly concerned with diagnostic pitfalls occasioned by this type of dysrhythmia. For decades simple forms of A-V dissociation have been erroneously interpreted by leading cardiologists as reciprocal rhythm (5, 6, 7) or complete A-V block (8, 9), and mistakes are, of course, more often made in casual circles. It is important to distinguish A-V dissociation from complete A-V block because complete block is usually an expression of serious irreversible heart disease, whereas A-V dissociation, though it may indicate a serious situation, is almost always evidence of a transient and reversible lesion. In complete A-V block, forward conduction does not and cannot occur, whereas in A-V dissociation forward conduction is always possible, although it may be impaired. In the electrocardiogram of complete block, three or four P waves are usually seen between the slow idioventricular complexes, whereas in A-V dissociation the atrial rate is usually a little slower than the ventricular; the dysrhythmia is, therefore, recognized by the fact that the P waves, being somewhat slower than the ventricular complexes, tend to "overtake" the QRS complexes (fig. 3A). When the P wave has emerged far enough beyond the ventricular complex so that the atrial impulse now reaches the conducting tissues and ventricles after their refractory period is over, a conducted beat results—so-called ventricular "capture."

It should be clear that in this dysrhythmia the primary upset is in the normal relationship between the rates of high and low pacemakers—the lower pacemaker (A-V nodal or ectopic ventricular) is beating faster than the atrial pacemaker, either because the lower pacemaker is abnormally excitable or because the atrial pacemaker is abnormally slow. When the dissociation is conditioned by slowing of the S-A node, the heart is often a normal one, but when it results from enhanced excitability of a lower pacemaker, it usually bespeaks an abnormal heart. In instances where the A-V node is in control of the ventricles at an abnormally rapid rate (70–120 per minute) the term nonparoxysmal A-V nodal tachycardia has been applied (10), and the underlying cause is commonly digitalis intoxication, rheumatic fever or inferior myocardial infarction.

Another form of dissociation is also frequently mistaken for complete A-V block. In the presence of atrial fibrillation, the ventricular rhythm is sometimes perfectly regular (fig. 3B). In these circumstances the ventricles are presumed to be under nodal or ectopic ventricular control and complete A-V block is often and unjustifiably inferred, although the ventricular rate may be in the neighborhood of 60-80 beats per minute. Mere absence of conduction is no proof of complete block. The most that can be inferred from this situation is that the ventricles are beating independently of the atria and that a form of A-V dissociation is therefore present; and that an enhanced excitability of the ventricular pacemaker is coupled with a sufficient degree of A-V block to prevent the fibrillating atria from controlling the ventricles. In other words, A-V dissociation has resulted because the automatic interval of the lower pacemaker is shorter than the refractory period of the conducting tissues.

University Hospital
Baltimore 1, Maryland
(*Dr. Marriott*)

Mercy Hospital
Baltimore 2, Maryland
(*Dr. Schamroth*)

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LEFT HEART CATHETERIZATION INDICATIONS AND TECHNIQUE

CHARLES J. McGAFF, M.D.*

Catheterization of the left side of the heart has become a commonly used technique. The information thus obtained is of proven usefulness and the procedure is reasonably safe. Left heart catheterization is particularly helpful in the evaluation of acquired lesions of the mitral and aortic valves and therefore is most commonly used in rheumatic heart disease.

Rheumatic fever may produce either stenosis or insufficiency of the mitral valve. When mitral stenosis exists, the valve orifice is narrowed and the leaflets become fixed. The valve cannot open fully in diastole and therefore affords an obstruction to the flow of blood from the left atrium to the left ventricle. This obstruction results in an elevation of the pressure in the left atrium, enlargement of this chamber and, eventually, pulmonary congestion. When the valve is insufficient there is no obstruction to the flow of blood from atrium to ventricle during diastole, and the valve remains more or less open during the whole cardiac cycle. The insufficient valve, remaining open during ventricular systole, allows the left ventricle to eject blood back into the atrium. This, of course, results in a rise in left atrial pressure and increases the amount of blood which must return to the left ventricle through the mitral valve during the next diastole. Thus, in mitral regurgitation, the amount of blood flowing across the mitral valve in diastole is increased.

The physical findings of mitral stenosis are well known and consist of a prominent right ventricular thrust and an insignificant apical impulse, a loud mitral first sound, an accentuated pulmonic component of the second sound, and the classic diastolic rumble. The rumble begins with the opening snap of the mitral valve and terminates with loud presystolic accentuation. The electrocardiogram in stenosis shows evidence of left atrial enlargement by widening and notching of the P waves, the so-called "P-mitrale." Right ventricular hypertrophy or incomplete right bundle branch block may also be found. X-ray examination usually shows prominence of the left atrium and pulmonary artery, and the right ventricle may appear enlarged. Small horizontal lines, the "B lines of Kerley," may be seen in the peripheral lung fields when the pulmonary venous pressure is high.

Mitral regurgitation in the pure state is manifested by a strikingly overactive and prominent left ventricular impulse at the apex, a loud apical holosystolic murmur radiating to the axilla and back, and the mitral first sound may be normal or diminished. A short mid-diastolic rumble may be heard at the apex due to the increased blood flow in diastole. X-ray examination may show a generalized cardiac enlargement, but the left ventricle is particularly prominent and the left atrium may be greatly enlarged. The electrocardiogram may reveal evidence of left ventricular hypertrophy.

A precise diagnosis is possible in the case of pure mitral stenosis or pure mitral regurgitation on the basis of these clinical findings alone. If the indications for surgery are present, patients with pure mitral stenosis can, and indeed should, be sent to operation without additional study. There are, however, certain situations in which left heart catheterization can be a useful adjunct to clinical evaluation of the patient with mitral valve disease.

1. When mitral stenosis and insufficiency coexist in the same patient, it is important to determine which lesion predominates. This decision is often difficult on clinical grounds alone. The importance of this determination of the predominant lesion is apparent if one considers that the valve with predominant stenosis is amenable to finger fracture, but the valve with predominant regurgitation will not be helped by this surgical procedure and may even be made worse. Surgical procedures for the correction of mitral insufficiency are currently in the developmental stage. All such procedures will require the use of the pump oxygenator; therefore precise preoperative diagnosis is essential.

2. Patients who have had previous mitral valve surgery may also present problems. Some of these become symptomatic after surgery and the possibility of inadequate surgical separation of the valve or "restenosis" must be entertained. Left heart catheterization is helpful in quantitating the amount of residual stenosis.

* National Foundation Fellow in Medicine. From the Departments of Medicine and Surgery, The Johns Hopkins Hospital.

3. The clinician may also be perplexed by the patient with symptomatic heart disease and a mitral diastolic murmur who has an atypical clinical course. In such a patient, the mitral stenosis may be an incidental finding and not hemodynamically significant, and the symptoms could be attributed to myocarditis. On the other hand, if the mitral stenosis is contributing to the patient's symptoms, it should be relieved.

In each of these situations the clinician is aware of mitral stenosis, but the laboratory is called upon to evaluate the physiologic and hemodynamic significance of this lesion. The laboratory must evaluate the degree of obstruction to blood flow produced by the lesion, and hence afford a basis for prediction of the outcome following surgical treatment. This information may be obtained by left heart catheterization.

The primary purpose of left heart catheterization in mitral valve disease is to obtain the mean left atrial pressure and to determine if there is a pressure gradient across the mitral valve in diastole. Pressures must be measured in both the left atrium and left ventricle. In a normal subject, the pressure in the left atrium is equal to that in the left ventricle at the end of diastole, i.e., there is no measurable end-diastolic pressure gradient across the normal mitral valve. The left atrial mean pressure may be obtained at right heart catheterization by wedging a catheter in a peripheral pulmonary artery, but the reproduction of the transmitted left atrial pressure waves is not good and, of course, nothing can be inferred about a gradient across the mitral valve. For these reasons left atrial puncture techniques were developed to obtain better and more direct information about the mitral valve.

There are four methods currently available for left atrial puncture:

1. *Dorsal Percutaneous:* (1) In this approach, the patient assumes the prone position and the left atrium is located by fluoroscopy. With local anesthesia, a no. 18 needle is inserted beside the vertebrae and passed medially until the atrium is entered. A small plastic catheter may then be passed through the needle into the atrium and manipulated until it crosses the mitral valve and enters the left ventricle. Simultaneous atrial and ventricular pressures may be recorded through the needle and catheter or consecutively through the catheter as it is pulled back across the valve. This dorsal puncture is through the pleura and therefore may be complicated by a pneumothorax or hemothorax and, in addition, has a small mortality. Rarely, a knot is accidentally tied in the catheter inside the atrium and must be removed by thoracotomy.

2. *Bronchoscopic:* (2, 3, 4) The patient is supine and the pharynx is anesthetized with a local anesthetic. The patient is bronchoscoped in the usual manner. The bronchoscope may be smaller than that used for diagnostic bronchoscopy. When the bifurcation of the trachea is visualized, a long no. 18 needle is passed through the bronchoscope and the left main stem bronchus is pierced about 1 cm. to the left of the carina. This area has been shown to be bacteriologically sterile. The needle passes through the bronchial wall and enters the left atrium. At this particular site there is no pericardium, and the pericardial cavity is usually not entered. A gauge for pressure measurement is attached to the needle. The existence of an atrial pressure tracing and high oxygen content in the blood withdrawn from the needle are used to confirm the fact that the needle is in the left atrium. A small plastic catheter may be passed through the needle and across the mitral valve. Simultaneous atrial and ventricular or consecutive pullback pressures may be recorded. The left ventricle is entered in the great majority of cases. When the mitral orifice is small or when the regurgitant jet is large, the catheter may not enter the ventricle. At times a more rigid plastic catheter may be used so it will not be washed back into the atrium with each regurgitant jet.

The bronchoscopic procedure is uncomfortable for the patient, but the stress seems to be well tolerated. The morbidity of the procedure is especially low, with no deaths directly attributed to it. Certainly the safety of the procedure far outweighs the slight discomfort.

3. *Transseptal:* (5) In this procedure a large cardiac catheter is passed up the saphenous vein of the supine patient. Its tip is positioned fluoroscopically in the right atrium against the interatrial septum. A long needle with a curved tip is passed through the catheter. The interatrial septum is pierced and the left atrium is entered. The pressure may be measured through the needle, or a fine plastic catheter may be passed through the needle into the left atrium. The left ventricle may be entered by the catheter and a pullback pressure recorded. In the small series so far reported, the left ventricle has been punctured

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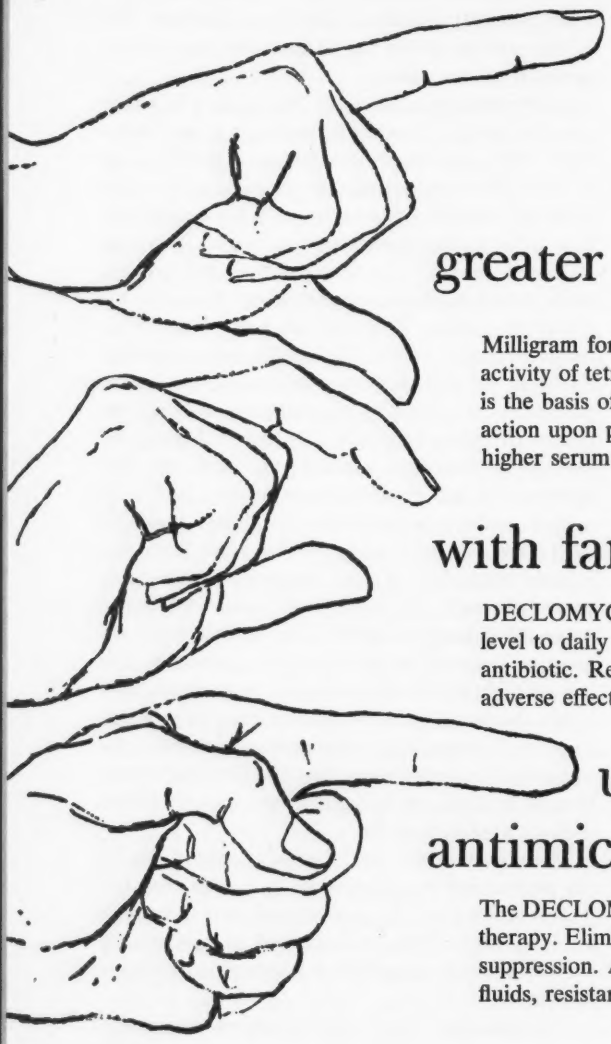

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4. *Substernal:* The patient, under local anesthesia, is placed in the supine position with the head extended. A long, fine needle is inserted in the suprasternal notch and guided through the anterior mediastinum. The aorta and pulmonary artery are penetrated and the left atrium is then entered. The left ventricular pressure must be obtained by anterior puncture (7).

The aim of the above procedures is to obtain the diastolic pressure on both the atrial and ventricular sides of the mitral valve. If a pressure gradient exists across the valve at a time in the cycle when the valve should normally be open, there is obstruction to the flow of blood and the magnitude of the gradient reflects the severity of the stenosis. This is an important determination and if the left ventricle is not entered from the left atrium, it should be punctured anteriorly to obtain its pressure.

A measurement of cardiac output is necessary at the time of the pressure measurements. The pressure gradient across a fixed orifice is directly related to the flow of blood, i.e., the higher the flow, the higher the gradient. A good estimate of the amount of regurgitation is also important since a mild stenosis with a large regurgitant volume may be associated with a diastolic mitral pressure gradient due to the increased flow. The information about the amount of regurgitation may be obtained from analysis of the atrial pulse contour or from indicator dilution curves.

A. *Atrial pulse contour:* When the mitral valve opens (at the peak of the "v" wave), there is a passive gush of blood from the atrium to the ventricle. This sudden emptying of the atrium is associated with a sharp fall in atrial pressure, the "y" descent. If there is obstruction at the mitral valve, as in mitral stenosis, this sudden gush of blood cannot occur through the small orifice and the pressure fall from "v" to "y" is slower than normal. This is shown in figure 1 from a patient with mitral stenosis. The "y" descent is normal or accelerated when there is a large regurgitant volume from ventricle to atrium and regurgitation is the predominant lesion. The predominant lesion is more apparent when the "y" descent is divided by the pressure of the "v" wave (8) or the mean left atrial pressure (9). Even better separation has been described when the rate of pressure fall of the "y" descent in the first tenth of a second is considered (9).

During ventricular systole when the mitral valve is closed, there is passive filling of the atrium from the pulmonary veins and a gradual rise in left atrial pressure to a peak, the "v" wave. If the mitral valve leaks during ventricular systole, this "v" wave may become quite accentuated and be proportionately much larger than the other atrial waves (10). Diastasis, a small rise in atrial pressure before the atrium contracts in sinus rhythm or before the ventricle contracts in atrial fibrillation, is an uncommon finding in a patient with predominant mitral stenosis. Its presence in the left atrial pulse can be interpreted as being against the existence of significant mitral stenosis (11). These waves and many other relationships in the atrial pulse (12) may be analyzed to give an idea of the dynamics of the valve.

B. *Indicator dilution:* During the left heart procedure, an indicator may be injected through the catheter and the subsequent dilution curve recorded from a peripheral artery for the determination of cardiac output. This measurement must be made in order to calculate the valve area (13) and to get some idea of the significance of the measured pressure gradient. The presence of valvular regurgitation distorts the dilution curve and an empiric analysis of the physical measurements of the curve may aid in the rough quantitation of the amount of regurgitation present. When regurgitation is present the dye is cleared from the heart more slowly than normal and this prolongs the curve, lowers the peak and delays the downstroke (slope) of the curve (14, 15). The relationship of these measurements to each other have been used to estimate the severity of any regurgitation present.

Another method currently in use for the assessment of mitral regurgitation is the injection of dye through a catheter in the left ventricle while sampling blood continuously from the left atrium (16). Normally dye injected into the left ventricle should not appear in the atrium, but if the mitral valve leaks, dye and blood will be regurgitated into the atrium and detected. This method is subject to some error due to present sampling techniques, the variability of the site of the sampling needle in relation to the mitral valve, and to the lack of complete atrial mixing of the dye. It does not give absolute quantitation of the regurgitant flow, but does give a reasonable estimate of its severity.

All of these methods may be used to obtain a

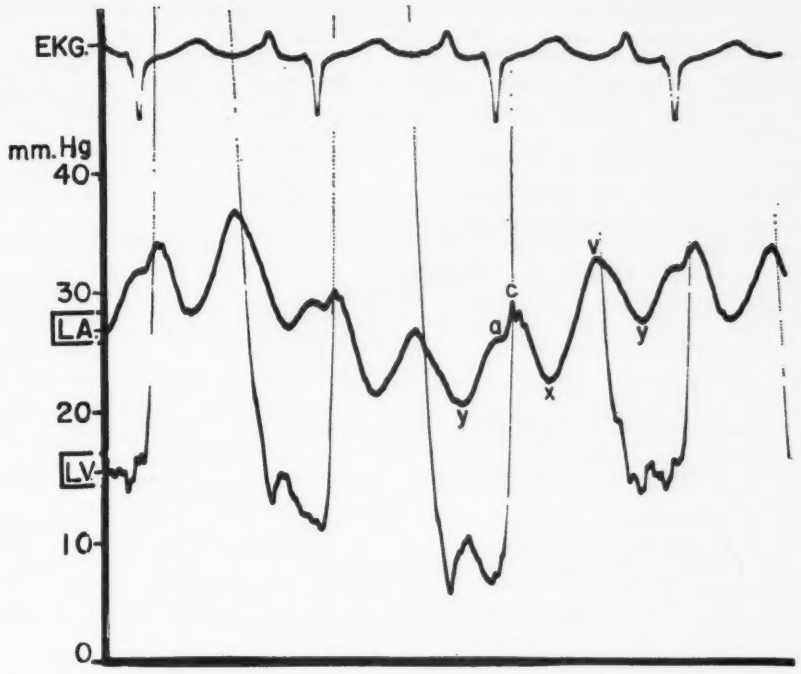

FIG. 1. Simultaneous left atrial (LA) and left ventricular (LV) pressures in a case of pure mitral stenosis. The systolic peaks in the ventricle were too high to be recorded at this sensitivity and only diastole is well shown. Note the pressure gradient throughout diastole between the left atrium and the left ventricle and the slow fall in pressure from "v" to "y".

ventricular pressure for the evaluation of the severity of aortic stenosis. The left ventricle may also be approached by passing a catheter up a systemic artery, through the aorta and across the aortic valve. A continuous pressure recording may be obtained while pulling the catheter across the valve. Often the catheter introduced into the ventricle from the atrium may pass into the aorta. Pullback pressure tracings in these instances may differentiate valvular from subvalvular stenosis. Cardiac output should also be obtained when the aortic valve is being evaluated. An indicator may be injected and the flow determined. Like mitral regurgitation, aortic regurgitation will also distort the dye dilution curve. Analysis of the curve may, therefore, give information regarding the severity of the regurgitation.

Left heart catheterization is also of value in those forms of congenital and acquired heart disease associated with left-to-right shunts (17, 18). If dye is injected into a normal left atrium and sampled from a peripheral artery, the dilution curve will have a sharp downstroke. If there is an atrial septal defect, the curve will not be as tall and the downstroke will be prolonged due to the slow release of dye from the central shunt. If dye is then injected into the left ventricle, the peripheral curve will be normal, thus demonstrating and localizing the site of the left-to-right shunt to the atrium. The same method can be applied for ventricular septal defects with left-to-right shunts by ventricular and aortic injections. An alternate method is to sample blood continuously from a catheter in the right heart chambers while an injection of dye is made into the left heart chambers (19). The early appearance of dye on the right side documents the presence and site of a left-to-right shunt.

Direct left ventricular puncture and retrograde left ventricular catheterization have been used for angiocardiography (20) and more recently for cine-angiocardiography with image intensification (21).

SUMMARY

Information derived from left heart catheterization is useful in the evaluation of certain patients with disease of the mitral and aortic valves. The procedure is indicated when it is necessary to evaluate the degree of organic stenosis in the presence of coexisting insufficiency, in the presence of coexisting myocarditis and following mitral commissurotomy.

The Johns Hopkins Hospital
Baltimore 5, Maryland

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Pertussis vaccine			Tuberculin test		
Tetanus toxoid			Smallpox vaccination		
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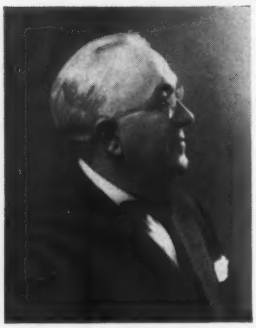
In Memoriam

Edward Philip Thomas, M.D.



Dr. Edward Philip Thomas, surgeon, one of Frederick's most prominent citizens and a leading figure in Maryland's medical circles, died unexpectedly at his home August 25, 1959. Death was attributed to a coronary occlusion and the news came as a distinct shock to the community.

While not in the best of health for some time, Dr. Thomas continued to carry on his customary professional duties. During his entire career it was an unusual occurrence for Dr. Thomas to miss a single day from his office or from making rounds at the Frederick Memorial Hospital. He administered to patients in his office until several hours before his death. He was truly dedicated to his profession; his services were always available to everyone and his close associates cannot recall an instance when he turned down a call. Those who knew him well considered him "a natural" in the practice of medicine. He had been deeply interested in medicine since his early school days when he used to accompany the late Dr. Thomas B. Johnson on his country calls.

Dr. Thomas was born in Buckeystown on February 26, 1892, a son of the late Newton and Sue L. (Mathias) Thomas of Frederick County. He received his M.D. from the University of Maryland in 1916 and served as a house officer at Church Home and Infirmary. War came and he began his public service as a military surgeon. A captain in the Army Medical Corps, he served overseas for three years. He was attached to Evacuation Hospital no. 3, A.E.F., and was on duty during and after battle and following the Armistice, with the occupation forces in Germany.

In 1920 Dr. Thomas, released to inactive status, returned to Frederick and began practice as a surgeon, in association with Dr. Thomas B. Johnson, a past president of the Faculty, and Dr. W. Meredith Smith. In addition to his wide surgical practice, Dr. Thomas was well known for his work in the field of traumatic surgery and x-ray.

In 1944 Dr. Thomas became chairman of the staff of Frederick Memorial Hospital and he served in this capacity for eight years.

In 1940 Dr. Thomas became President of the Medical and Chirurgical Faculty of Maryland. He had previously served as president of the Frederick County Medical Society. He was a member of the Maryland State Board of Medical Examiners from 1937 until 1954 for 17 years and served from June 6, 1944 until June 4, 1946 as president of this Board. Dr. Thomas was a Fellow of the American College of Surgeons and served on the Credentials Committee. He was also a diplomate of the American Board of Surgery.

Dr. Thomas was a member of the Evangelical Reformed United Church of Christ.

Aside from his professional interests, Dr. Thomas was active in various Masonic bodies. He was a member of Columbia Lodge No. 58, A.F. and A.M.; Enoch R.A. Chapter No. 23, Enoch Council No. 10 R. and S.M.; Jacques deMolay Commandery No. 4 K. T.; Ali Ghan Temple A.C.N.O.M.S. and Jesters of Ali Ghan Temple.

Dr. Thomas was also a member of Frederick Lodge, No. 684, B. P. O. Elks; the Fishing Creek Rod and Gun Club; the Frederick County Fish and Game Protective Association, Inc.; and the Francis Scott Key Post No. 11, American Legion.

He was a charter member of the Frederick Kiwanis Club and at the time of his death was an honorary member of that organization, as well as an honorary member of the Frederick Lions Club. Dr. Thomas was also a member of the Columbia Country Club and of the Alfalfa Club of Washington, D.C.

Dr. Thomas married the former Louise G. Firmin, daughter of Mr. and Mrs. George Firmin, of Glenside, Pa., a graduate of Swarthmore College. One of their sons, Robert, is a physician. Another son, Edward Jr., is news and sports director of Station WSLS, Roanoke, Va. The daughter, Louise, a trained nurse, is the wife of Dr. Denton Cooley, a prominent Houston surgeon.

Possessing a winning personality and a genial and amiable disposition, Dr. Thomas acquired a wide circle of friends in all walks of life, national and state, as well as local levels. His prime interest was in his

family and his profession, but his true greatness was in the service he gave beyond the "call of duty" for his patients, associates, and friends.

The final paragraph of an editorial in the Frederick News aptly sums up the feeling of our community for Dr. Thomas:

" 'Dr. Eddie,' as he was affectionately called, endeared himself to countless persons during the many years of his professional career. He gave unselfishly of his time and talents. Few men could claim as many devoted friends. He will always be remembered for his kindly, lovable manner and generous spirit. His memory will long be revered."

A. Austin Pearre, M.D.

William T. Hammond, M.D.

RESOLVED, that the entire membership of the Medical Staff of the Memorial Hospital at Easton, Md., Inc., adopt these resolutions in tribute to the memory of our late fellow member and distinguished colleague, William T. Hammond.

The Medical Staff has lost by death many distinguished and beloved members. No one is more genuinely mourned by the professional rank and file in the sense of a personal loss to such an extent as Doctor Hammond.

By his death we have lost a beloved associate whose outstanding character and humanitarianism reflected high honor upon our profession and whose memory is a worthy inspiration for the future.

It is fitting that we should record Doctor Hammond's personal qualities as they were revealed to the members of our staff in our daily associations. His was a sterling character. Its genuineness was reflected in his gentlemanly demeanor at all times, his high-minded sense of duty to his profession and to the public, his unselfishness, his kindness, his understanding and his wholesome good fellowship.

When his plans for an X-ray Department were formulated he undertook the task with enthusiasm and a fixed determination that the finest possible service to the community be established.

It is known that he was influenced by a strong spiritual feeling and he brought to every decision a sense of fairness which made his counsel much sought.

Doctor Hammond was appointed to the staff in 1912, and for nearly 47 years devoted much of his effort, generosity and energy to advancing the quality of medical care for our community. He served as secretary, chief of the medical staff, as well as chief of the Department of Radiology. He also served as president of his county and state medical societies. He was a diplomate of the American Board of Radiology and a member in the American Medical Association, Maryland Radiological Society, Radiological Society of North America, Southern Medical Association, American College of Radiology, and The Medical and Chirurgical Faculty of Maryland.

A life such as his cannot end without a sense of loss to those who have been intimately associated with him. His memory will be a priceless possession for his children and for the multitude of friends who knew him and loved him.

RESOLVED, that a copy of this resolution be transmitted to the family of the deceased and to The Medical and Chirurgical Faculty of Maryland.

The Medical Staff
Memorial Hospital at Easton, Md., Inc.
John N. Robinson, M.D., Secretary
J. T. B. Ambler, M.D., Chief of Staff

MARYLAND LICENSES GRANTED

The following physicians, having passed an examination given by the Board of Medical Examiners of Maryland, were granted license to practice medicine and surgery in the State of Maryland as of July 21, 1959:

Abramson, David Leavitt
Adler, Wolfe N.
Aliapoulios, Menelaos Anastasios
Altemus, Armin Joseph
Ances, Isadore George
Anderson, Joel William, Jr.
Anderson, Joseph E., Jr.
Arizaga, Jose Rolando
Ashburn, William Lee
Asrael, Gerson
Baltzan, Betty Lou Ray
Barker, Lewellys Franklin II
Barnes, Barrington Benton
Bledsoe, Turner
Borodajko, Lubomir
Branch, James Christian
Branna, Pasquale
Brown, Charles Coady
Brown, Richard Osborne
Bryant, D'Orsay Deavenport
Bublitz, Deborah Keirstead
Burkholder, Paul Kurtz
Bych, Myroslav Merrell
Cadden, John Francis, Jr.
Capestany, Roberto A.
Cardines, Richard Joseph
Chang, James Chi
Choate, John Wellington
Cholmondeley, Horace Ivelaw
Church, Gerard
Clarendon, Colin Campbell Dixon
Clowry, Lawrence John, Jr.
Cohen, William Nathan
Cone, Donald Frank
Connor, Audley Francis, Jr.
Cotter, Julian Ray
Coursey, John William
Courts, Donald Earle
Cox, Clyde Bolyn, Jr.
Crawford, Jerry
Czebotari, Alexander Leopold
Dahbura, Anton
Dana, Alan S., Jr.
Darr, Joseph L.
Dawson, Robert J.
DeMaio, Enrico F.
Demarco, Salvatore J., III
Dismond, Samuel R., Jr.
Douglas, Florence M.
DuBose, John M.
Dunseath, William J. R.
Durkan, James P.
Dyer, Bernard C.
Esterly, John R.
Evke, Abdullah
Ewy, Herbert G.
Falls, William F., Jr.
Farley, Francis E.
Feinberg, Gilbert N.
Felsenberg, Stanley Z.
Fesus, Andre
Fletcher, Charles B.
Flores-Herta, Jose
Flory, Clyde R., Jr.
Fortin, Victor L., Jr.
Fox, Thomas E.
Freeman, Harold P.
Gallager, Wilmer K., Jr.
Gallagher, George C.
Gamse, Norman L.
Gardiner, Theodore D.
Glazier, Jon B.
Grant, Kingsley B. J.
Graves, Joseph G.
Green, Karl M.
Greene, Herbert H.
Greene, John R.
Grollman, Arthur P.
Haase, Gunter R.
Halle, Carlton I.
Harris, Louis C., Jr.
Hastings, Alicia E.
Hill, William E.
Holder, Henry H.
Holt, Robert S.
Hudson, John W.
Hunter, James G., Jr.
Ingham, Roger B.
Irwin, Robert C.
Isaacs, Gilbert H.
Jackson, Frank W., II
James, Robert T.
Janovski, Nikolas A.
Jarboe, James P.
Jasion, Arthur R.
Jones, Arthur F., Jr.
Jones, Leroy
Jones, Marion E.
Jones, Thomas K., Jr.
Joyce, Eugene E.
King, August D., Jr.
Kirsh, Marvin M.
Kleinman, Martin S.
Kraut, William
Lang, Richard C.
Lasser, Norman L.
Lenhard, Raymond E., Jr.
Lew, Hea R.
Lewis, Donald R.
Lewis, Jack C.
Losemann, Heinrich J.
Madden, Arthur A.
Mailman, Charles J.
Mainolfi, Ferdinand G.
Mapp, Esmond M.
Mapp, Yolanda I. J.
Marder, Victor J.
Maresca, Glanco M.
Marshall, Lewis West
Mau, Richard D.
McDaniel, James B., Jr.
McDowell, Milton K.
McGovern, John M.
McKay, Elmer S.
McWilliams, Donald R.
Mengoli, Louis R.
Mildvan, Patricia T.
Moore, Francis E., Jr.
Mower, Morton M.
Murphy, Robert J.
Musavi, Sadredin
Naib, Zuher M.
Natale, Ralph D.
Nataro, Joseph F.
Newcomb, Richard W.
O'Malley, William E.
Otto, Joseph R., Jr.
Ozelis, Sophie
Palmieri, Frederick, Jr.
Pattison, Joseph H.
Phillips, Theodore J.
Pinkner, Lawrence D.
Pitts, William H., Jr.
Poffenbarger, Arthur L.
Prado, Oscar Garcia
Plotkin, Gerald R.
Rauh, Jay Thomas
Reda, Mario J.
Rhea, William E.
Ribner, Herbert
Rubenstein, Howard J.
Russo, Gerard L.
Rybczynski, Carol E.
Schocket, Stanley S.
Sera, Carlos C.
Serpick, Arthur A.
Shields, Earl F., Jr.
Snyder, Stanley N.
Starr, Henry J.
Stump, Beverly J.
Thomas, Robert T.
Tourian, Ara Yervant
Trail, Mervin L.
van der Veen, Teunis
VanderVeldt, Albert J.

Varner, Robert I.
Voiss, Daniel V.
Webb, Ozella T.
Whitehead, Richard B.
Wiggins, Henry W., Jr.
Wilhelmsen, Hans R.
Wizenberg, Morris J.
Wood, Colin
Wuerker, Raymond B.
Yee, Jason F.
Young, Robert H., Jr.

The following physicians have been licensed to practice medicine and surgery in the State of Maryland by virtue of reciprocity:

July 2, 1959

Atwood, John Morris, Missouri

July 17, 1959

Buchanan, Lee Kruidenier, Colorado
Gold, Martin Irvin, National Board
Locke, Robert Vincent, National Board
Miller, David Israel, Indiana
Sheer, Walter Benjamin, California
Shultz, Charles Richard, California

July 28, 1959

Ray, Catherine T., National Board
Rivat, Georte Louis, National Board
Rose, Lawrence, National Board
Sawada, Edward Akira, Virginia

August 14, 1959

Young, James Kent, National Board

September 15, 1959

Ball, Wilmot Coles, Jr., National Board
Bowen, Mary Elizabeth, Missouri
Braverman, Elliot Martin, National Board
Burgerman, Arthur, Indiana
Ciminello, Vito John, National Board
Connor, Charles David, North Carolina
Corn, Milton, National Board
Cruet, Jorge Perez, National Board
Cunningham, Alice Norida, California
Davis, Thomas Bruce, Wisconsin
Dubroff, Seymour, National Board
Faulstick, Dyrel Alden, National Board
Hepner, Walter Ray, Jr., California
Hewson, William, Pennsylvania
Johnson, Tillman Davis, Pennsylvania
Jones, Thomas Christopher, Tennessee
Kaiser, Irwin Howard, National Board
Kieffer, William Joseph, Iowa
King, Walter Bradley, Jr., California
O'Connell, Joseph Patrick, Pennsylvania
Parker, Caddie Lewis, National Board
Santina, Henry, Georgia
Schleifer, Carl B., Georgia
Siegel, Charles Isaac, National Board
Smith, Ray Manson, Louisiana
Steenburg, Richard Wesley, Massachusetts
Waldmann, Katharine Emory Spreng, Massachusetts
Wickner, Ira, New York

SINAI HOSPITAL MOVES

Sinai Hospital of Baltimore, Inc. moved from its present location at Monument Street and Rutland Avenue to its new quarters at Belvedere Avenue at Greenspring on December 13, 1959.

Located on a 50 acre site in northwest Baltimore, the new Sinai Hospital has 483 beds and 91 bassinets. Built at a cost of $20,000,000, it includes a separate research building, medical staff residence, school of nursing, and nurses' residence. The expanded outpatient and emergency room facilities are designed to handle 100,000 outpatient visits a year. There are 119 ward beds, with no more than two patients to a room, except in pediatrics. All patient areas are air conditioned.

The teaching and research programs will remain in close association with the Johns Hopkins University.

A special scientific dedication is planned for Saturday and Sunday, April 23 and 24, 1960

Component Medical Societies

ALLEGANY-GARRETT COUNTY MEDICAL SOCIETY

LESLIE E. DAUGHERTY, M.D.

Journal Representative

Allegany County Medical Museum

Rene Laennec was a surgeon in the French Civil War in 1799, the same year as the founding of the Medical and Chirurgical Faculty. Born in 1781 and graduating from medical school in 1804, he attained immortality at the age of 35, when he invented the stethoscope in 1816.

Today, there is displayed in the medical section of the Allegany County Historical Society the first stethoscope to reach the western shore of Maryland. Brought here by one of the founders of the Faculty, Dr. George Lynn, it is a monument to Laennec. Devoted to studying diseases of the chest, he eventually fell ill with tuberculosis and died, but not until he had described every sound within the heart and lungs.

A hundred years after the founding of the Medical and Chirurgical Faculty, Dr. Arthur Hansen Hawkins, the seventy-second president of the Faculty, located in Mt. Savage and brought with him an early vaginal speculum. A pioneer in surgery, Dr. Hawkins later became the leading surgeon of Western Maryland, where he practiced from 1907 to 1952.

Air Force Medical Officer Addresses Medical Society

A dinner meeting of the Allegany-Garrett County Medical Society was held at the Cumberland Country Club, on October 8, with the doctors' wives present. Speaker of the evening was Lt. Col. Norman I. Condit, United States Army Air Force Medical Corp. Dr. Condit's subject was "Space Medical Research," illustrated by a film titled "Vertical Frontier." Following the scientific session, the regular business meeting was held.

Personals

Dr. D. B. Grove, Dr. Carlton Brinsfield and Dr. Earl R. Paul, of Cumberland recently attended the

Fig. 1. Ivory and Ebony Stethoscopes—Early Vaginal Speculum (Allegany County Medical Museum).

American College of Surgeons' Meeting in Atlantic City, N. J.

Dr. Hilda Jane Walters, Frostburg, Md. and Dr. Abraham Mirkin, of Cumberland, Delegates of the Allegany-Garrett County Medical Society attended the Semiannual Meeting of the Medical and Chirurgical Faculty in Ocean City. Also attending from Cumberland were Dr. and Mrs. James T. Johnson, Jr.

Dr. W. Royce Hodges, Cumberland, attended a meeting of the Flying Physicians' Association held September 7–11 at Western Hills Lodge, Sequoia State Park, Tulsa, Oklahoma.

The following officers were elected by the staff of Memorial Hospital, Cumberland. President: Dr. Samuel M. Jacobson, Vice President, Carlton Brinsfield, Secretary: Dr. Frank T. Cawley. Elected to serve on the Joint Conference Committee were Drs. Harold W. Eliason and Wylie M. Faw.

ANNE ARUNDEL COUNTY MEDICAL SOCIETY

SAMUEL BORSSUCK, M.D.

Journal Representative

The Anne Arundel County Medical Society met at the Officers' Club of the United States Naval

Academy on September 16, 1959. This was a joint meeting with the Anne Arundel County Bar Association. Mr. James C. Morton, president of the County Bar Association, in his introductory remarks suggested that the medical society have a financial committee to decide on court fees for physicians. Dr. Hodes, of Philadelphia, and Dr. Abel, of San Francisco, gave a most interesting discussion of "Whiplash Injuries." Dr. Bohlman, of the staff of the Anne Arundel General Hospital in Annapolis, monitored a question and answer period during which a number of interesting medical and medicolegal points were discussed.

Dr. Edmond Moushbek's application for membership in the society was accepted.

National Diabetic Week was brought to the attention of the society, and members were urged to participate in the diabetic detection drive.

A cardiac symposium, sponsored by the Heart Association of Maryland, to be held in November at the United States Naval Hospital in Annapolis, was called to the attention of the society.

BALTIMORE CITY MEDICAL SOCIETY

CONRAD ACTON, M.D.
Journal Representative

The winter season of the City Medical Society began promptly on Tuesday, September 8, with a meeting of the Executive Board. Complaints by insurance carriers regarding excessive charges were considered by the board as a whole acting as a Grievance Committee, instead of the usual three-man procedure. The secretary was directed to tell the insurance representative that the individual had been censured after exhaustive investigation of the charges.

A report of the Committee to Study the Allocation of Blue Shield Fees, Dr. Francis Gluck, chairman, was referred, in turn, to the State Faculty and higher levels of the State administration.

A resolution from the pharmacists concerning the desirability of omitting the names of ingredients of prescriptions on labels was discussed. Considered a matter with great variation of individual preference, it was decided that each physician should be permitted to handle this matter as he desired.

A recurring suggestion that an honorarium for out-of-town speakers be provided was presented by the Program Committee. The Executive Board felt that this was not in order. While there was never any question about expenses incurred in the visit, the Treasurer Dr. Kimberly stated that he issues checks promptly for whatever is requested in this matter of transportation. Offering an honorarium was not considered appropriate in our Society.

Dr. Whitehouse spoke of the importance of the Grievance Subcommittee of the Executive Board, which he declared is one of the most important areas where the *official* medical organization comes in contact with the public. He urged all members of the subcommittee to give immediate and careful attention to cases that come before them and especially to consider the public relations aspect involved.

Dr. Samuel Morrison's letter urging the appointment of a chairman for the Baltimore City representative to the House of Delegates was given thought. Failure of communication between the Executive Board and its delegates has been a matter of concern to some Board members for some time. It was recalled, however, that the delegates, in the past few years, had elected their own chairman. In the absence of a direct constitutional provision, the delegates are powers to themselves. The Executive Board, since they are excluded as delegates, should not seem to influence the delegates in any way, but should make available to the delegates information concerning the Executive Board's policies in regard to any matter upon request. The Executive Board voted to continue in this manner, and leave the delegates' internal arrangements to themselves; however, President Whitehouse said he would take this matter up at the projected meeting with the delegates on Friday, September 11.

The first meeting of the Baltimore City Medical Society for the 1959–60 season was held Friday,

October 2. President Samuel Whitehouse called the meeting to order promptly at 8:30 P.M. After the minutes were read and approved and 99 new members were elected by voice vote, the scientific part of the program was presented.

President Whitehouse, recalling that we have had 11 speakers from Boston address us during the past 10 years, introduced Dr. Oliver Cope, associate professor of surgery at the Harvard Medical School, who spoke on "Diagnosis and Management of Hyperparathyroidism: Experience Harvested in the Treatment of 225 Cases since 1932."

Dr. Cope, in his fresh, crisp manner, described the historical origin of his interest in parathyroid surgery. Noting that "the only way I can present it is the way I saw it," he declared his early dedication to surgery was channeled to an interest in the parathyroids while associated with Drs. Aub, Allbright, and Walter Bauer, at the Massachusetts General Hospital.

Dr. Cope developed the widening knowledge of the effect of disturbed calcium metabolism: how hyperparathyroidism was first considered a bone disease, then a kidney disease. Later it was associated with duodenal ulcers and, most recently, has been suspected in states of extreme fatigue, pancreatitis, mental states with aberrations of judgment, in mild hypertension, and even in transient cerebral-vascular accidents. This widened area of influence of hyperparathyroidism was surprising to many.

Regarding surgical extirpation, he described the differing embryology of the upper and lower parathyroids. The two upper ones are associated primarily with the thyroid; the two lower ones are embryologically identified with the thymus. His x-rays and illustrative slides were most enlightening.

Following the brief paper, Dr. William F. Rienhoff spoke of the tremendous work Dr. Cope had done in bringing out the embryogenesis of the glands. Dr. John Eager Howard, claiming "never to have won any arguments from Cope," felt he should say that there was always some other condition chemically suspect to mimic parathyroidism. He declared that until an assay of the parathyroid hormone in serum was available, differentiation of primary and secondary hyperparathyroidism would always be in doubt. In his reply, Dr. Cope felt it wasn't fair to have such warm friends discuss his paper. He admitted that the pathologist cannot tell the difference between primary and secondary hyperparathyroidism and that surgery amounted to a diagnostic tool for the differentiation of the condition.

After the departure of Dr. Cope and the nonvoting portion of the audience, a business meeting was held. Dr. Roderick Shipley introduced a resolution regarding the recommendations made to Baltimore hospitals by the Residency Review Committee in Internal Medicine concerning the employment of an internist as full-time director of medical education. After the enumeration of eight particulars, it was resolved that the Baltimore City Medical Society urge the involved hospitals to "disregard" these recommendations. He introduced a resolution that certain requirements be made of future inspectors of these hospitals.

The unexpected resolution was sufficient to nonplus the audience until Dr. Classen took the floor to protest that the Baltimore City Medical Society has no right to advise hospitals to "disregard" the recommendations of any properly constituted inspecting agency.

Drs. Howard and Diggs agreed that the members of the Society should have sufficient time to digest the various whereases and wordings of the resolution before its presentation for the Society's full approval. Dr. Diggs requested that the resolution be referred to the Executive Committee to report back to the next meeting of the Society. Dr. Pierpont agreed it would be more democratic to defer to the constituted authorities; however, Dr. Samuel Morrison objected that the authorities in Chicago should be informed promptly before their committee representatives start making additional demands on small hospitals. In his opinion, requiring small hospitals to meet the qualification of a teaching hospital, which they are not able to do, is grossly unfair.

Dr. Wilgis spoke concerning his experience with such rating committees, stating his opinion that the hospitals want freedom of action without pressure either way. He also urged delay and review of the wording of the resolution to be sure it expressed what it was meant to express. To President Whitehouse's inquiry why there should be such a great rush to put the resolution through, Dr. Mosberg replied that the purpose of the resolution was to encourage the smaller hospitals to maintain their good standards within their capabilities. Dr. Pierpont again questioned whether, if the Society should pass the resolution as it was presented on this night, the Executive Board had any right to change even a word or a comma. After considerable parliamentary juggling, it was referred to the Executive Board for consideration and return to the Society at the next meeting for action.

Following the meeting coffee, doughnuts and cocoa were served to the large group who had stayed.

BALTIMORE COUNTY MEDICAL ASSOCIATION, INC.

WILLIAM H. F. WARTHEN, M.D.
Journal Representative

At the monthly luncheon meeting of the Baltimore County Medical Association, held at the Stafford Hotel in Baltimore on September 23, the vice president, Dr. Margaret Lee Sherrard, presided. President, Dr. J. Morris Reese, was absent, due to his attendance at a meeting of the Advisory Board of Health of Baltimore County.

Dr. Martin K. Gorten, assistant professor of pediatrics at the University of Maryland School of Medicine, was the speaker. He chose as his topic, "New Concepts of Therapy in Blood Disorders of Children." Dr. Gorten stressed the therapeutic aspects of blood disorders of children and enlarged upon the splendid research study now being conducted in the blood dyscrasias of children at the University of Maryland School of Medicine and at the University Hospital. A most enlightening question and answer period followed Dr. Gorten's presentation of the subject.

Dr. Sherrard brought to the attention of those present a letter from Dr. I. Ridgeway Trimble, chairman of the Committee on National Emergency Medical Services of the Medical and Chirurgical Faculty of the State of Maryland. Dr. Trimble asked that an active cooperation program be inaugurated by the Baltimore County Medical Association and the Director of Medical Services of Civil Defense in Baltimore County. He pointed out the need to encourage at an early date an active participation by the private physicians of Baltimore County with the Division of Medical and Health Services of Baltimore County in forming an administrative and training cadre for the 200-bed Civil Defense Emergency Hospital now stored in Baltimore County. Dr. William H. F. Warthen, who is director of Medical and Health Services for Civil Defense in Baltimore County, recommended that Dr. Trimble be the speaker at an early meeting of the Baltimore County Medical Association, and that the program be devoted entirely to the subject of participation by physicians in Civil Defense. It was recommended that the meeting include Mr. Sherley Ewing, director of the Maryland Civil Defense Agency, and Mr. William P. Bolton, director of all Civil Defense activities in Baltimore County.

Dr. John A. Engers and Dr. Eugene Blank were received into active membership, and Dr. William C. Ebeling was received into affiliate membership in the Baltimore County Medical Association.

FREDERICK COUNTY MEDICAL SOCIETY

LOUIS R. SCHOOLMAN, M.D.
Journal Representative

The September meeting of the society was held at the Francis Scott Key Hotel on the 15th. The speaker of the evening was Dr. Robert Coffey, professor of surgery at Georgetown University. His talk on surgery of peptic ulcer was absorbing and stimulating. Having heard Dr. Coffey speak before the society on pancreatitis several years ago, we were expecting something special, and were not disappointed.

At the October meeting of the active staff of the Frederick Memorial Hospital, Dr. Leonard

Scherlis, associate professor of medicine and head of the Department of Cardiology, was guest lecturer. He gave a well organized and most practical talk on preoperative workup of the cardiac patient.

MONTGOMERY COUNTY MEDICAL SOCIETY

CHARLES FARWELL, M.D.

Journal Representative

Dr. DeWitt DeLawter presented an interesting scientific resume of the oral hypoglycemic drugs at our monthly dinner meeting at Norbeck Country Club.

Our annual dinner dance meeting was a highlight of the social season in our medical community. Dr. James Roberts and Mrs. Ostman were responsible for its success at Indian Spring Country Club. Many members enjoyed themselves so much at the Indian Spring Club, that consideration may be given to making it the meeting place for our monthly scientific sessions.

Now that our membership includes nearly 400 physicians, obtaining a place large enough to accommodate us all with wives and friends is requiring more planning.

Active discussion has focused on several items affecting Maryland physicians: (1) proposed architectural changes of the Maryland Faculty building in Baltimore, (2) registration every two years of everyone licensed to practice medicine and surgery in Maryland, (3) consideration of employing an assistant executive secretary by the Maryland Medical and Chirurgical Faculty.

Selected numbers of us are contributing our time and services to a pilot study of the mental health needs of the Montgomery County citizenry and the methods of diagnosis and treatment of psychiatric problems in our community.

WICOMICO COUNTY MEDICAL SOCIETY

RAYMOND M. YOW, M.D.

Journal Representative

Wicomico County Medical Society resumed its monthly meeting schedule on September 14, 1959, after a summer recess. Three new physicians were accepted for membership: Dr. Gladys Allen, who has recently opened her office for the practice of obstetrics and gynecology; Dr. Robert Adkins, who has opened his office for the general practice of medicine in Fruitland; and Dr. Joseph Fitzgerald, who was transferred from the Baltimore City Medical Society and has recently opened his office for the practice of internal medicine.

The guest speaker for the evening was Dr. Robert H. Shaw, chief of the cardiovascular laboratory and member of the Department of Surgery of Massachusetts General Hospital. Dr. Shaw discussed acute arterial insufficiency, and his discussion was illustrated with slides. Following the meeting refreshments were served.

At the October 12 meeting, the guest speaker was Dr. Brice S. Vallett of Wilmington, Delaware. Dr. Vallett discussed diseases of the prostate and illustrated with slides and colored motion pictures his technique for performing transsacral prostatectomy.

The business portion of the meeting was presided over by Dr. Theodore Smith, vice president, in the absence of the president, Dr. Hunter Mann.

Personalities

Dr. Hunter H. Mann and Dr. Frank E. Poole are convalescing at their homes after undergoing minor surgery recently.

Dr. Raymond M. Yow was recently admitted to Fellowship in the American College of Surgeons during their recent clinical congress, October 2, 1959.

PLAQUE HONORS LATE DR. BENJAMIN SARUBIN

A plaque in honor of the late Dr. Benjamin Sarubin, chief of surgery at Doctors Hospital from 1951 until shortly before his death on April 23, 1959, has been placed in the lobby of the hospital.

Placed immediately below a portrait of Dr. Sarubin, the plaque reads as follows:

"In honor of Benjamin Sarubin, M.D., chief of surgery, Doctors Hospital, 1951–1959 whose skill, devotion, and humanity contributed beyond measure to the service of the hospital's patients, its staff, and its future."

Born in Russia, the late Dr. Sarubin migrated to Baltimore in his boyhood. He was a graduate of Baltimore Polytechnic Institute and George Washington University. A surgeon since 1930, he served on the staffs of Lutheran, Franklin Square and South Baltimore General Hospitals, in addition to his post at Doctors Hospital.

SIR WILLIAM OSLER, BART.

(1849–1919.)

BY PEDHAMMOX

A twelvemonth has pass'd since thy brave spirit fled,
Its tenement, earthly, deserting
For realms of sweet bliss, where the quick and the dead
To their Master's image, reverting.
Sad, sad grew our hearts when the message so brief,
(Both time and chill winter defying,)
America, reach'd, that our hero, "The Chief,"
Within a land distant lay dying.
Serene, withal beautiful, thy great life's close,—
A star in the east, stately setting!
Humanity's voice, in due homage, arose
Demise thine, untimely, regretting.
We miss thee, Sir William! Thy counsels divine,
Real tenets of action acquiring;
The charm of thy voice and thy presence benign,
The best then within us inspiring.
Welch, Osler, and Kelly, immortal each name,
With Halsted*—redoubtable cluster!
On Johns Hopkins school shedding excellent fame,—
Unfading, untarnishing luster.
Oh! thou wert the first of this world-famous band,
Full tribute to Dame Nature paying;
Though cold be thy relics, unnerv'd be thy hand,
Thy worth we, in vain, are essaying:
Of diagnosticians, "Prince;" clinics, "The Chief;"
In art and in science excelling;
Attention quick gain'd, thy discourse e'en but brief,
Thy splendor of diction compelling.
Beyond the St. Lawrence whose turbulent tide,
Its wealth of wild grandeur disclosing,
On Canada's soil—his lov'd birthplace, his pride,
His ashes so fondly reposing;
Pray, there let him rest, 'neath the dew and the snow,
'Mid hearts his good deeds have made lighter;
In silence he sleeps, yet his name it shall grow—
And fame, too—increasingly brighter.
Then, hail and adieu! to our mentor, "The Chief,"
His shining example extolling;
Though long be the years and unbidden our grief,
His tomb, hence, a Mecca consoling.

* Reference is here made to the justly celebrated portrait-group of the Four Doctors—William S. Halsted, Howard A. Kelly, William Osler, and William H. Welch, painted by John S. Sargent, R.A. in 1905.

EDITOR'S NOTE—This month marks the fortieth anniversary of the death of Sir William Osler, which occurred at Oxford, England, December 29, 1919. These stanzas were written in commemoration of the first anniversary of his death. Our thanks go to Mrs. Maud Carrigan, of the staff of the Medical and Chirurgical Faculty, for submitting this for Journal publication.

Obituaries

H. Roland Carroll, M.D.

1894–1959

And may there be no moaning of the bar, When I put out to sea—Tennyson

Dr. H. Roland Carroll himself "put out to sea" on September 7, after being physician and friend to thousands of seamen in his capacity as director of the Custom House out-patient annex of the United States Public Health Hospital. He was 65 and had retired last year.

A native Baltimorean, Dr. Carroll graduated in 1917 from the University of Maryland Medical School. He interned at Mercy Hospital, after which he spent two years in the Army Medical Corps, serving with the 80th Division.

Upon his return from European duty, Dr. Carroll assumed his post of director of the Custom House medical facility, which he held for 39 years until his retirement.

Dr. Carroll was one of the organizers of a Baltimore society known as the Fair and Warmer Club. He was a thirty-second degree Mason.

He is survived by his wife, Frances, and daughter, June.

August L. Ewald, Jr., M.D.

1906–1959

Injuries received in a fall caused the death of Dr. August L. Ewald on September 20. He was 53.

Dr. Ewald graduated from the University of Maryland School of Medicine in 1935. He interned at Maryland General Hospital, where he later became a staff member, serving as visiting physician.

The Baltimore surgeon saw action during World War II as head of a Seabee battalion medical unit. He was wounded on Okinawa by Japanese shrapnel a week after the Japanese had surrendered.

Dr. Ewald was a member of the Faculty and the A.M.A. through the Baltimore City Medical Society. He was also a Mason, a Shriner and a member of the Flint Club.

His wife, Audre, and two children, Mrs. Joann Spier and Gordon A. Ewald, are survivors.

William Thomas Hammond, M.D.

1886–1959

His sudden death on July 10, 1959 ended Dr. William T. Hammond's 47 years of medical practice in Easton. He was a native Eastern Shoreman, having been born 73 years ago in Berlin, Maryland.

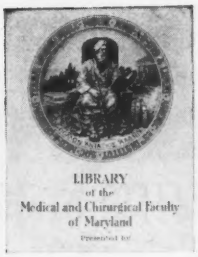
Dr. Hammond graduated from Hahnemann Medical School in 1909 and remained in Philadelphia for a year of hospital training. He returned to Berlin in 1911 to start a general practice, joining the Medical and Chirurgical Faculty the same year.

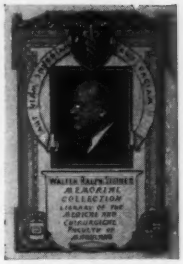
He moved his practice to Easton in 1912 where he remained active until his death. Dr. Hammond became vitally interested in x-ray work and was certified by the American Board of Radiology.

Dr. Hammond was elected president of the Faculty for the year 1947. During his years of practice in Talbot County he was president of the County Medical Society, chief of staff of Memorial Hospital and, at the time of his death, chief of radiology. He was a member of the A.M.A., Southern Medical Society, Maryland Radiological Society, American College of Radiology and Radiological Society of North America.

A widower, Dr. Hammond is survived by two children, William T. Hammond, Jr. and Mrs. Charles Elliott Wheeler, both of Easton, a brother and four grandchildren.

H.F.K.





Library

Louise D. C. King *Librarian*

"Books shall be thy companions; bookcases and shelves, thy pleasure-nooks and gardens." *Ibn Tibbon*

New Books

Adams, Mark H.	Bacteriophages. N. Y.	1959
Adriani, John	Fundamentals of general anesthesia for students and practitioners of dentistry. Springfield	1959
American Public Welfare Association	Public Welfare directory. Chic.	1959
Arrington, G. E.	History of ophthalmology. N. Y.	1959
Bailey, Hamilton	Emergency surgery. 7th ed. Balt.	1958
Barkan, Hans, tr. & ed.	Johannes Brahms and Theodore Billroth—letters. Okla.	1957
Bean, W. B.	Vascular spiders and related lesions of the skin. Springfield	1958
Behrens, Charles F.	Atomic medicine. 3d. ed. Balt.	1959
Bernier, Joseph L.	Management of oral disease. St. Louis	1959
Bluemel, Elinor	Florence Sabin. Univ. Col. Pr.	1959
Blumenthal, Herman T.	Pancreatitis. Springfield	1959
Boies, L. R.	Fundamentals of otolaryngology. Phil.	1959
Bradley, O. C.	Topographical anatomy of the dog. 6th ed. N. Y.	1959
Carton, Charles A.	Cerebral angiography in the management of head trauma. Springfield	1959
Cecil, R. L.	Textbook of medicine. 10th ed. Phil.	1959
Coffin, Kenneth B.	The medical secretary. N. Y.	1959
Cook, James	Remedies and rackets. N. Y.	1958
Cooper, Linn F.	Time distortion in hypnosis. Balt.	1959
Cummins, N. M.	Some chapters of Cork medical history. Cork (Ireland)	1957
DeWitt, Clinton	Privileged communications between physician and patient. Springfield	1958
Dornette, William H.	Instrumentation in anesthesiology. Phil.	1959
Dowling, Harry F.	That the patient may know. Phil.	1959
Dunham, Charles L.	Radioactive fall-out: a 2 year summary report.	1959
Dunn, L. C.	Heredity and evolution in human populations. Bost.	1959
DuVries, Henri L.	Surgery of the foot. St. Louis	1959
Elek, S. D.	Staphylococcus pyogens and its relation to disease. Balt.	1959
Elkins, H. B.	Chemistry of industrial toxicology. N. Y.	1959
Fried, B. M.	Tumors of the lung and mediastinum. Phil.	1958
Friedman, A. P.	Headache: diagnosis and treatment. Worcester, Mass.	1959
Goldberger, E.	Water, electrolyte and acid-base syndromes. Phil.	1959
Gollan, Frank	Physiology of cardiac surgery. Springfield	1959
Grabill, Wilson H.	Fertility of American women. N. Y.	1958
Greene, N. M.	Physiology of spinal anesthesia. Balt.	1958
Grossman, Louis I.	Handbook of dental practice. Phil.	1958
Hall, Peter F.	The functions of the endocrine glands. Phil.	1959
Hollender, M. H.	The psychology of medical practice. Phil.	1958
Homburger, F., ed.	Physiopathology of cancer. 2d. ed. N. Y.	1959
Hughes, E. S. R.	Surgery of the colon. Livingston Edin.	1959
Jackson, Chevalier, ed.	Diseases of the nose, throat and ear. 2d ed. Phil.	1959
Jamar, J. M., ed.	International textbook of allergy. Springfield	1959
Jordan, E. P., ed.	The physician and group practice. Chic.	1958
Keys, Ancel and Margaret	Eat well and stay well. Garden City	1959

Kinney, William A.	Medical science and space travel. N. Y.	1959
Knowles, J. H.	Respiratory physiology and its clinical application. Cambridge, Mass.	1959
Lamm, Stanley S.	Pediatric neurology. N. Y.	1959
Licht, S., ed.	Therapeutic electricity and ultraviolet radiation. New Haven	1959
Lovett, Ethelbert	An approach to ethics. Balt.	1958
McIlwain, Henry	Biochemistry and the central nervous system. 2d. ed. N. J.	1959
McLaughlin, H. L.	Trauma. Phil.	1959
Marti-Ibañez, Felix, ed.	History of American medicine.	1959
Marti-Ibañez, Felix	Men, molds and history.	1958
Merritt, H. Houston	Textbook of neurology. 2d. ed. Phil.	1959
Moritz, Alan R., ed.	Trauma and disease: selections from the recent literature. N. Y.	1959
Morrison, L. R.	The effect of advancing age upon the human spinal cord. Cambridge, Mass.	1959
Moss, W. T.	Therapeutic radiology. St. Louis	1959
Moyer, John, ed.	Hypertension. Phil.	1959
Myers, J. Arthur	A history of the American College of chest physicians, 1935–1959. Chic.	1959
Myers, J. Arthur, ed.	Tuberculosis and other communicable diseases. Springfield	1959
Najjar, Victor A.	Immunity and virus infection. N. Y.	1959
Nelson, Waldo E.	Textbook of pediatrics. 7th ed. Phil.	1959
Neustatter, W. L.	Psychiatry in medical practice. N. Y.	1959
Nock, Albert Jay	Snoring as a fine art and 12 other essays. N. H.	1959
Nybakken, O. E.	Greek and Latin in scientific terminology. Ames	1959
Pack, George T., ed.	Treatment of cancer and allied diseases: v. 3 Tumors of the head and neck. N. Y.	1959
Paul, Lester W.	Essentials of roentgen interpretation. N. Y.	1959
Pendergrass, E. P.	The pneumoconiosis problem, with emphasis on the role of the radiologist. Springfield	1959
Prior, J. A.	Physical diagnosis. St. Louis	1959
Ranson, Stephen W.	Anatomy of the nervous system. Phil.	1959
Reid, Mary E.	The guinea pig in research: biology, nutrition, physiology. D. C.	1958
Riese, Walther	History of neurology.	1959
Riley, Gardner M.	Gynecologic endocrinology. N. Y.	1959
Roques, F. W., ed.	Diseases of women. Balt.	1959
Ruch, Theodore C.	Diseases of laboratory primates. Phil.	1959
Russell, W. Ritchie	Brain, memory, learning. N. Y.	1959
Sakel, Manfred	Schizophrenia. N. Y.	1958
Sarton, George	History of science v. 2 Bost.	1959
Schneck, Jerome M., ed.	Hypnosis in modern medicine. 2d ed. Springfield	1958
Scott, W. G. & Evans, T.	Genetics, radiobiology and radiology. Springfield	1959
Selye, Hans	Chemical prevention of cardiac necroses. N. Y.	1958
Sheppard, P. M.	Natural selection and heredity. Quakertown, Pa.	1959
Siemens, H. W.	General diagnosis and therapy of skin diseases. Chic.	1958
Singleton, E. B.	X-ray diagnosis of the alimentary tract in infants and children. Chic.	1959
Sternberg, Thomas H., ed.	Modern dermatologic therapy. N. Y.	1959
Stevenson, L. G.	Meaning of poison. Kansas	1959
Stookey, Byron	Trigeminal neuralgia. Springfield	1959
Sutherland, V. C.	Synopsis of pharmacology with special application to dentistry. Phil.	1959
Tiecke, Richard W.	Pathologic physiology of oral disease. St. Louis	1959
Trout, Robert	Practical evaluation of surgical heart disease. N. Y.	1959
Turell, Robert	Diseases of the colon and anorectum. Phil.	1959
Turner, Dorothea	Handbook of diet therapy. Chic.	1959
Walker, R. Milnes	Pathology and management of portal hypertension. Balt.	1959
Weil, Paul G.	Plasma proteins, clinical significance. Phil.	1959
Weyrauch, Henry M.	Surgery of the prostate. Phil.	1959
Winsor, Travis	Peripheral vascular diseases. Springfield	1959
Zimmerman, H. A., comp. ed.	Intra vascular catheterization. Springfield	1959

Maryland
SOCIETY OF PATHOLOGISTS
INC.

LOUIS B. THOMAS, M.D., *President*

EDWARD C. McGARRY, M.D., *Secretary*
Suburban Hospital, Bethesda, Md.

THE USE OF RADIOISOTOPES AS A DIAGNOSTIC AID

The pathology laboratory is rapidly undergoing changes to provide more accurate diagnosis of various conditions. One change is the use of radioactive isotopes in laboratory diagnostic procedures. Examples of the use of radioactive isotopes to provide the diagnosis of different pathologic states are as follows:

Thyroid Disease

The measurements of radioactive iodine uptake in the thyroid gland and the production of protein bound radioactive iodine in the blood are well established methods for evaluating thyroid function. The excretion of radioactive iodine in the saliva and the estimation of tri-iodothyronine uptake by the patient's red cells are new tests which may prove useful in estimating thyroid function. Scanning apparatus may locate malignant thyroid tissue in the neck and in the mediastinum if the tissue takes up iodine. Within the tissue so located areas of hypo- or hyperactivity may be identified.

Anemias

Estimation of iron stores and determination of rates of red cell production and red cell destruction can be made with radioactive iron.

Radioactive iron can be used to study the ability of the intestinal tract to absorb iron in patients with iron deficiency anemia.

Blood Volume Studies

Iodine tagged serum albumin can be used to determine the plasma volume which may indicate the transfusion needs of surgical patients. Plasma volume studies are also useful in the diagnosis and management of patients with polycythemia.

Red Cell Survival Studies

The life span of red cells can be determined by tagging the red cells with radioactive chromium. Hemolytic anemias may be identified by this technique.

Pernicious Anemia

Pernicious anemia can be diagnosed in patients with the disease even when they are in complete remission. Vitamin B_{12} tagged with radioactive cobalt given by mouth will not be absorbed in pernicious anemia patients except when given with intrinsic factor. Collection of urine following the administration of tagged vitamin B_{12} with and without intrinsic factor can differentiate pernicious anemia from other macrocytic anemias.

Space Occupying Lesions of the Liver

Following the administration of Rose Bengal tagged with radioactive iodine scanning apparatus may be used to identify the presence of space occupying lesions in the liver.

Pancreatic Function Studies

Some information of pancreatic function may be obtained by the oral administration of glycerol trioleate tagged with radioactive iodine. The degree of digestion of this fat can be determined by taking counts on the blood and stool. Pancreatic disease may be differentiated from intestinal steatorrheas by the comparison of the results of this test with the results of the oral administration of I^{131} tagged oleic acid and I^{131} tagged serum albumin.

MEDICOLEGAL SYMPOSIUM

on

ALCOHOL TESTING UNDER MARYLAND'S NEW LAW

(Breathalyzer Demonstration)

Osler Hall

January 28, 1960—8:00 P.M.

Moderator: Hon. John E. Raine, Judge, Circuit Court, Baltimore County

Panel Participants:

Henry C. Freimuth, Ph.D., Toxicologist, Office of Chief Medical Examiner of Maryland
"Correlation of Alcohol Levels With Behavior"

Lt. William V. Elliott, Wilmington, Delaware Police Department
"Demonstration of Performance, Tests and the Breathalyzer Analysis for Alcohol"

Theodore C. Waters, Jr., Esq., Baltimore, Maryland
"Legal Aspects of the Provisions of Maryland's New Chemical Test Law"

This meeting should be of special interest to all physicians since the new law contains a paragraph providing "The person tested shall be permitted to have a physician of his own choosing administer a chemical test in addition to the one administered at the direction of the police officer." The Committee has arranged this symposium in order that physicians may be familiarized with the procedures to be used by the Baltimore City and Maryland State Police in alcohol testing and with the procedures they as physicians might use if called upon in accordance with the above quoted paragraph.

The Heart Page

Gordon Walker, M.D. – Coeditors – Robert Singleton, M.D.

A SERVICE OF

THE HEART ASSOCIATION OF MARYLAND

FREE PATIENT SERVICES AVAILABLE TO PHYSICIANS

through the Heart Association

WORK CLASSIFICATION UNIT

Helps determine the work potential of persons with cardiovascular disease and attempts to re-establish them in employment through available community resources.

VISITING OCCUPATIONAL THERAPIST

Provides: interesting activities during enforced leisure, activities to increase independence and work tolerance, and prevocational training

EQUIPMENT LOAN SERVICE

Lends hospital beds, wheel chairs and bedside equipment without charge where purchase or rental works a hardship.

RHEUMATIC FEVER PROPHYLAXIS

Penicillin for the prevention of recurrences of rheumatic fever. Available for two cents per day or free, based on patients ability to pay.

VISITING RECREATIONAL THERAPIST

Provides interesting activities for homebound children through craft work, monthly newspaper, and special activities.

CAMPING

Provides camping opportunities for cardiac children. Both regular and restricted programs are available.

WORK SIMPLIFICATION

Group instruction in energy conservation for housewives with heart disease who must limit their activities in caring for their homes and families.

INFORMATION-REFERRAL

To help locate sources of help for patients

MEDICAL SOCIAL WORKER

Assists cardiac patients in solving problems related to cardiovascular disease.

PATIENT EDUCATION MATERIALS

Provide materials written especially for cardiovascular patients to promote a better understanding of cardiovascular diseases and the importance of following preventive and therapeutic schedules (available in quantity to physicians).

LOW SODIUM DIET BOOKS

A guide for the patient on a low sodium diet (not a cookbook)
Available in 500 mg., 1000 mg., and mild sodium restriction
15 cents per copy.

BALTIMORE CITY HEALTH DEPARTMENT

HUNTINGTON WILLIAMS, M.D.
COMMISSIONER

P. O. Box 1877 Baltimore 3, Md. PLaza 2-2000: Extension 307

Learn To Do Your Part In The Prevention Of Disease

LEAD PAINT KILLS SECOND CHILD IN 1959

By October 15, 61 cases of lead paint poisoning had occurred in teething children in the poorer sections of Baltimore City. Two of these resulted in death. This brings to a total of 124 the number of children that have died from lead paint poisoning since 1931, when the Baltimore City Health Department began fighting this scourge. Of this number, 44 were white children and 80 were Negro.

Baltimore City Health Department records show that 795 children—167 white and 628 Negro—are known to have suffered from lead paint poisoning in Baltimore. In 1958 alone, 133 children became ill and 10 died.

The death of the second child in 1959 should serve as a grim warning to parents not to wait for symptoms to develop, but to take a child at once to a doctor or Health Department clinic if he is seen eating paint or chewing on a painted surface. Parents who wait may be too late.

Other cities are studying Baltimore's control efforts in the matter of lead paint poisoning. In Cincinnati, for example, there have been 54 cases of lead paint poisoning in 1959, and a leading pediatrician in the University of Cincinnati College of Medicine recently wrote for copies of the Baltimore City ordinances and other information on the control of this often fatal illness.

Signs and symptoms of this kind of lead paint poisoning are:

Chewing at the window sill
Increasing listlessness
Pains in the abdomen
Frequent nausea and vomiting
Persistent constipation
Irritability
Frequent headache
Convulsions

Formerly, a great number of convulsions in two year old children and some subsequent deaths were without clear diagnosis or explanation of etiology. It is now believed that a fair number of these were the result of lead paint poisoning.

Huntington Williams, M.D.

Commissioner of Health

TRUDEAU SOCIETY FORMED IN MARYLAND

An organizational meeting of the Maryland Trudeau Society was held in Baltimore on October 16. The state society is an affiliate of the American Trudeau Society, medical arm of the National Tuberculosis Association. Its work in Maryland will be carried out in conjunction with the program of the Maryland Tuberculosis Association.

Dr. Richard L. Riley of the School of Hygiene and Public Health was elected to serve as the Society's first president. Dr. Moses S. Shiling was elected vice president. Dr. Shiling is a Maryland representative director to the National Tuberculosis Association. Other officers elected were Dr. Meyer W. Jacobson, diredtor of the Division of Tuberculosis, Baltimore City Health Department, secretary-treasurer; and Dr. Leon H. Hetherington, chief of the Tuberculosis Division, Maryland State Health Department, representative councilor to the American Trudeau Society. Dr. William S. Spicer, chief of the Pulmonary Diseases Section, University of Maryland Medical School, and Dr. Edmund G. Beacham, chief of the Tuberculosis Division, Baltimore City Hospitals, were elected to serve on the Executive Committee.

MARYLAND TUBERCULOSIS ASSOCIATION
Christmas Seal Agency for State of Maryland
900 ST. PAUL STREET • BALTIMORE 2, MARYLAND

THE JOHNS HOPKINS HOSPITAL CHEST CLINIC

LULU M. HAROUTANIAN, M.D.* AND
WARDE B. ALLAN, M.D.†

Tuberculosis continues to be a serious problem in Maryland, especially in the poorer areas of Baltimore. The Chest Office is consulted continuously by the Department of Medicine and other departments of the hospital about the diagnosis of doubtful cases and the treatment and disposal of patients with proven tuberculous lesions. Through the Chest Office, every effort has been made to maintain close contact and excellent cooperation between the hospital and the various agencies dealing with tuberculosis in the State of Maryland. This cooperation is a pleasant feature of the clinic's work and is in great measure due to Doctor Miriam Brailey's endeavours in the past few years.

In addition to the work with tuberculous patients, the Chest Office is concerned with teaching nursing students, medical students and house staff, administering two chest clinics a week, organizing a weekly chest conference and correlating the clinical and respiratory function aspects of chest disease in the hospital.

Teaching

Student teaching is conducted at the chest clinics, which are held twice weekly, and on weekly ward rounds attended by visting chest physicians. These formal ward rounds are in addition to numerous informal consultations held on the wards every day. The teaching of the early recognition of tuberculosis and the details of differential diagnosis to students and interns is an integral part of the tuberculosis program.

* Instructor in medicine, instructor in environmental medicine, Johns Hopkins Hospital.

† Physician-in-charge, Chest Clinic, Johns Hopkins Hospital.

Chest Conferences

At the weekly chest conference the more complicated chest cases in the hospital and clinics are seen and discussed. These conferences are attended by students, the house staff and the physicians practicing outside the hospital and provide a forum for discussion and management of chest disease in all its aspects.

Mass Radiography

This unit was disbanded during the summer. Several years ago the Maryland Tuberculosis Association provided the Johns Hopkins Hospital with a photo-fluorographic x-ray unit for the use of patient admissions and employees. As Dr. Russell H. Morgan, radiologist-in-chief, stated in a letter to Mr. Frank Jones, executive director, Maryland Tuberculosis Association, the unit provided "long and faithful service and has been of immeasurable value to those physicians concerned with chest disease. As the photo-fluorographic unit grew older it appeared increasingly desirable to replace it with more modern apparatus." At this instance it seemed more suitable to do the examinations previously conducted on the photo-fluorographic unit on regular 14 x 17 inch films. It has been affirmed by the Chest Office and by Dr. Morgan, in whose department the survey work will be continued, that "the work instituted under the banner of the Maryland Tuberculosis Association will be continued." The disbanding of the unit has not led to any diminution in the number of consultations for suspected tuberculosis nor to any lessening in demand for the Chest Office services.

Respiratory Function Studies

During the past two years a strenuous effort has been made to bring closer together the work of the chest clinicians with that of Dr. Richard Riley's

group of respiratory physiologists. Studies are made of the respiratory function of patients being followed clinically for various chronic diseases, including tuberculosis, and the results are helpful in the management of these patients as well as gaining an understanding of their underlying disease. The Chest Office has played a large and increasingly active part in this collaboration.

The chest clinic program is used directly in the service of tuberculous patients and in the study and management of the wide spectrum of chronic lung disease as seen in the Johns Hopkins Hospital.

All these services are supported by a grant from the Maryland Tuberculosis Association. This grant, as are all similar grants given by the Association, is made possible by the traditional Christmas Seal Campaign which is conducted annually during the six week period preceding Christmas Day.

CALENDAR OF EVENTS

THURSDAY, DECEMBER 10

NEUROPSYCHIATRIC SECTION, B.C.M.S.
in cooperation with the Maryland Association of Private Practicing Psychiatrists
6:30 P.M. Dinner Meeting The Seton Psychiatric Institute

"Rival Psychotherapy"

Dr. Francis Joseph Gerty, Chicago, Illinois, past president of the American Psychiatric Association and visiting professor of psychiatry at the Seton Psychiatric Institute.

FRIDAY, JANUARY 8

BALTIMORE CITY MEDICAL SOCIETY
8:30 P.M. 1211 Cathedral Street

SATURDAY, JANUARY 9

TELEVISION PROGRAM, B.C.M.S.
5:00 P.M. WMAR-TV, Channel 2
"Nursing as a Profession"—Miss Ruth Preston, R.N., Mrs. Teddy Kares, R.N., Dr. Martin L. Singewald

TUESDAY, JANUARY 12

PEDIATRIC SECTION, B.C.M.S.
6:00 P.M. Dinner Sheraton Belvedere
8:30 P.M. 1211 Cathedral Street

BALTIMORE EAR, NOSE & THROAT SOCIETY
6:15 P.M. University Club

Woman's Auxiliary Medical and Chirurgical Faculty

MRS. E. RODERICK SHIPLEY *Auxiliary Editor*

DECEMBER, 1959

WELCOME ALLEGANY-GARRETT WOMAN'S AUXILIARY

During the past summer a lot of ground work was done in Allegany and Garrett Counties by the State Membership-At-Large chairman, Mrs. A. J. Mirkin, Cumberland, Md., for the organization of an auxiliary.

On July 2, 1959, the wives held a luncheon meeting for the purpose of organizing an auxiliary. Mrs. Mirkin, acting as temporary chairman, explained the aims and purposes of an auxiliary. Mrs. Carlton Brinsfield was appointed temporary secretary. At the suggestion of Mrs. H. M. Eliason, a committee consisting of Mrs. Leland Ransom and Mrs. Thomas F. Lewis was appointed to consult with the county medical society for its approval of the formation of such an auxiliary.

Pending the report of approval, it was suggested that Mrs. W. A. Van Ormer and Mrs. James G. Stegmaier act as a nominating committee for the group's officers; Mrs. Samuel Jacobson, Mrs. Wyand Doerner and Mrs. Abdul S. Hashim to comprise a welcoming and hospitality committee for new doctors' wives in the two counties; Mrs. E. I. Baumgartner and Mrs. Robert Feddis to serve as coordinators for the mental health and education program; and Mrs. A. J. Mirkin to tackle the bylaws.

Arrangements for the meeting were made by Mrs. Lewis, assisted by a telephone committee consisting of Mrs. James Hallinan, Mrs. Brinsfield and Mrs. William Iames. Since Mrs. Brinsfield was appointed temporary secretary, Mrs. Ralph Reiter offered to serve in her capacity on the telephone committee. Mrs. G. Overton Himmelwright volunteered to send notices of the next meeting.

The organizational meeting was held on September 30, 1959 with a luncheon at the Cumberland Country Club. Mrs. Mirkin, the temporary chairman, conducted the meeting.

Explaining the aims and purposes of the auxiliary as community service and medical education, Mrs. Mirkin quoted Dr. Louis Orr, president of the AMA, "To me, one of the greatest functions the woman's auxiliary can perform is to act as an educational force in medicine. It is essential that you do not underestimate your value to the medical profession, because you are a most valuable asset."

The constitution was presented and accepted. During the formative period, it was decided to meet the second Wednesday of each month, and later quarterly.

The officers elected were: Mrs. Thomas Lewis, president; Mrs. E. I. Baumgartner, vice president; Mrs. G. Overton Himmelwright, secretary; Mrs. Ralph Reiter, treasurer, and Mrs. A. J. Mirkin, advisor to the board. Others attending were: Mrs. Ralph Ballin, Mrs. E. E. Broadup, Mrs. Leslie Daugherty, Mrs. Wyand Doerner, Mrs. H. W. Eliason, Mrs. Robert Feddis, Mrs. James Hallinan, Mrs. Abdul Hashim, Mrs. Samuel Jacobson, Mrs. Emmett Lee Jones, Mrs. Lloyd R. Meyers, Mrs. Mikio Kato, Mrs. Leslie R. Miles, Mrs. R. Rett Rathbone, Mrs. Blaine Schindler, Mrs. Benedict Skitarelic and Mrs. William Van Ormer.

It was my pleasure to be in attendance at this last meeting along with President-elect Mrs. William S. Stone and Parliamentarian Mrs. Albert E. Goldstein. I am grateful for all of the fine work that went into this project, and I am proud to present our newest county auxiliary to you. Let's welcome them and hope that other unorganized counties will join with us in our efforts to assist our doctors.

Mrs. D. Delmas Caples
President, Woman's Auxiliary to
the Medical and Chirurgical Faculty

SEMIANNUAL MEETING

The day dawned bright, sunny and warm in Ocean City for our Semiannual meeting. We would like to think that everyone came for business, with play thrown in for good measure, but fear many came for a day at the seashore with no thought of attending a meeting. However, much to the delight of the officers and committee chairmen, the business meetings were well attended.

The proceedings were opened by Mrs. D. Delmas Caples, our president. All assembled were pleased to hear the reading of a letter from the Faculty advising that a room had been made available exclusively for the Auxiliary, complete with a secretary when needed. We gratefully thank the doctors for making conditions much more pleasant and efficient to work with and for them.

One of the nicest reports was the news that Allegany-Garrett had set the date of September 30 for completing the organization of an auxiliary. Mrs. A. J. Mirkin, who served as chairman for the organization, has also found members from three other counties who will serve as members-at-large chairmen in their respective areas where no auxiliaries exist.

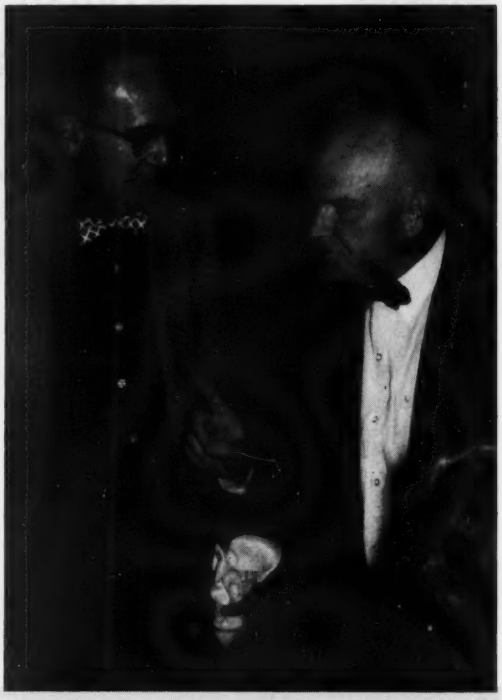
The selection of a nominating committee was the major business of the morning meeting. The members selected are:

Mrs. Emil G. Bauersfeld, Montgomery County, *Chairman*
Mrs. Walter M. Hammett, Baltimore County
Mrs. Jacob G. Warden, Washington County
Mrs. Merritt Robertson, Carroll County
Mrs. Leslie E. Daugherty, Allegany County

Every one is invited to send to this committee her selection for next years officers, provided the nominee has given her consent to have her name placed on the ballot and she is a member of the Auxiliary in good standing.

Following the business meeting a round table conference was held. Everyone was invited to join one of the groups and to take part in the discussions. State chairmen, representing their own topics, served as leaders for the groups; county chairmen and guests were the participants. The subjects under discussion were Finance, Recruitment, Legislation, A.M.E.F. Civilian Defense and Parliamentarian.

If the results could be judged by the obvious interest and steady hum of voices, the conference was a huge success. It is good to get together and talk out the ideas that are brought forth at such a gathering. This has been only our second conference meeting; yet its value is a real one. In order to make greater use of the contribution each individual can bring to us, we need to communicate freely and informally. Let there be bigger and better conferences as we grow.



Dr. Leslie E. Daugherty, Faculty president, explaining to Dr. Asa Dougal Young while luncheon is in progress.

A delightful smorgasbord luncheon was enjoyed in the dining room of the Commander Hotel. Many felt quite disappointed that the clam bake on the beach was dispensed with this year, but there was much pleasant chatter and loads of vanishing food to prove that the party was, after all, a success.

The Faculty sponsored a most enjoyable evening of dancing and provided hors d'oeuvres to wind up this annual affair.

Many families stayed for a weekend of bathing, fishing or just plain loafing.

We will look for you to join us at this traditional spot on the Chesapeake Bay when we meet again next September. If you haven't been in attendance yet, you just don't know how profitable and how much fun it can be.

Mrs. Robert C. Kimberly, Mrs. Amos Koontz and Dr. Robert C. Kimberly attending smorgasbord luncheon.

Mrs. George E. Urban, Mrs. Charles H. Williams, Mrs. Robert C. Kimberly and Mrs. Martin E. Strobel chatting at conference.

Mrs. D. Delmas Caples, president, transacts some business.

Mrs. William S. Stone, president-elect conducting round-table.

INTRODUCING OUR COUNTY PRESIDENTS

Mrs. John H. Rehberger

Dolores Rehberger is serving her second term as president of the Woman's Auxiliary to the Baltimore County Medical Association. She has formerly served as vice president and program chairman of the County Auxiliary, having been active in the Auxiliary since 1955. A past membership chairman of the State Auxiliary, she is now fourth vice president of the State Auxiliary, as well as state hospitality chairman.

Dolores first met her husband, Dr. John M. Rehberger, while she was in the School of Nursing of the Hospital of the University of Pennsylvania. Her husband then was senior resident in otolaryngology and bronchoesophagology of the same institution and instructor in the School of Medicine of the University of Pennsylvania. She now enjoys assisting her husband in the care of his patients.

Mrs. Rehberger was formerly president of the Sunnybrook Homemakers' Club in Baltimore County. While in Germany with Dr. Rehberger, she was hospitality chairman of the Wurzburg Woman's Club.

Dolores has a great deal of pleasure in raising an active young son of eight years. She enjoys copper enameling, painting, sewing, collecting rare pieces of china and traveling.

PRESIDENT'S TRAVELOGUE

Your president, Mrs. Caples, attended the Annual Conference of Presidents and Presidents-elect in Chicago in October. She was also a guest of the Delaware and Pennsylvania State Medical Auxiliaries during their annual meetings, and the guest of Prince George's County Auxiliary at its September meeting, thus performing her duty of visiting each county auxiliary at least once during her term of office.

SOUTHERN MEDICAL AUXILIARY

The Woman's Auxiliary to the Southern Medical Association held its thirty-fifth annual meeting in Atlanta November 16–18, in conjunction with the Southern Medical Association. Mrs. John M. Chenault was installed as president at the conclusion of the sessions.

Mrs. Ross Z. Pierpont, of Baltimore City, is the Maryland representative of the Southern Medical Association Auxiliary.

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for quick, effective relief

Antiallergic, antispasmodic, demulcent
Reduces bronchial spasm and congestion
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Ambodryl® hydrochloride (bromodiphenhydramine hydrochloride, Parke-Davis)	24 mg.
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Dihydrocodeinone bitartrate	⅙ gr.
Ammonium chloride	8 gr.
Potassium guaiacolsulfonate	8 gr.
Menthol	q.s.
Alcohol	5%

Supplied: Bottles of 16 ounces and 1 gallon.

Dosage: Every three or four hours—adults, 1 to 2 teaspoonfuls; children, ½ to 1 teaspoonful.

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†Analysis of clinical reports.

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Howard M. Bubert—1962
Albert E. Goldstein—1962
Amos R. Koontz—1962

EASTERN DISTRICT
Howard F. Kinnamon—1961
John Mace—1962

SOUTHERN DISTRICT
Arthur Wooddy—1960
Philip Briscoe—1960

SOUTH CENTRAL DISTRICT
M. McKendree Boyer—1960
Waldo B. Moyers—1961

Terms of office expire at conclusion of annual meeting

DELEGATES TO THE AMERICAN MEDICAL ASSOCIATION

Delegate	*Alternate*
Robert vL. Campbell—1959	William B. Long—1959
George H. Yeager—1960	H. Hanford Hopkins—1960
J. Sheldon Eastland—1961	William B. Hagan—1961

Terms of office expire at end of calendar year

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VOLUME 8 | *December, 1959* | NUMBER 12

CONTENTS

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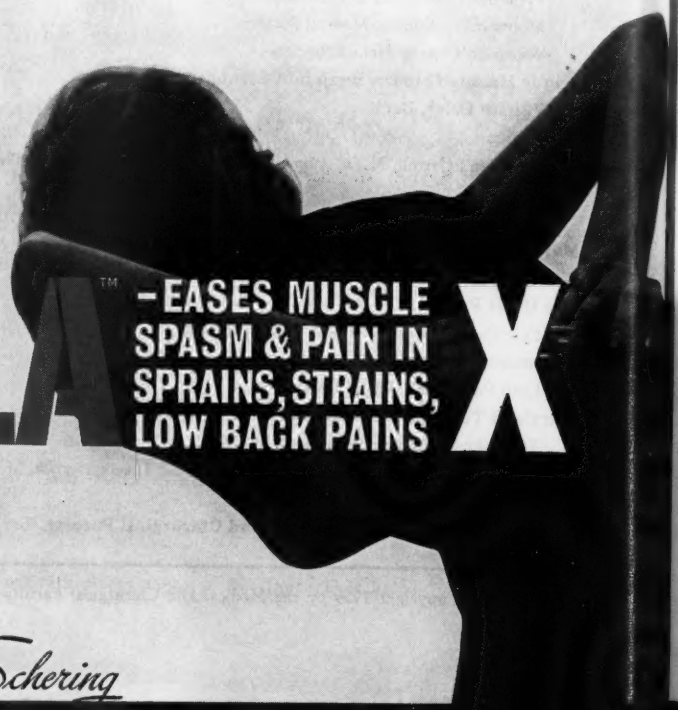

[X]MYOGESIC
muscle relaxant – analgesic

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EXECUTIVE SECRETARY'S NEWSLETTER

December, 1959

PERSONALITIES

Dr. Otto C. Phillips has been named a member of the American Society of Anesthesiologists; Dr. George L. Morningstar has commenced the practice of general medicine in Emmitsburg; Dr. Victor F. King has moved to Towson from Catonsville; Dr. Allan C. Barnes has been appointed professor and director of the Johns Hopkins Hospital Department of Gynecology and Obstetrics; Dr. Arthur T. Keefe, Jr., Chestertown, has been named a Fellow of the American College of Surgeons; Dr. Julius N. Cahn has been elected a member of the American Medical Writers Association; Dr. Arthur Woodward has been named Chief of Surgery at the Montgomery County General Hospital, and Dr. M. McKendree Boyer has been named Chief of Staff; Dr. Richard L. Riley has been elected President of the Maryland Trudeau Society; Dr. Ray Hepner has been named Professor of Pediatrics at the University of Maryland School of Medicine; and Dr. John R. Smith, Jr., began general practice in Centreville.

SPEAKERS

Dr. Jerome Frank at Homewood Friends Meeting; Dr. Edward F. Lewison at a symposium in New York on the Evaluation of Early Diagnosis of Cancer; Dr. Harold Rosen at the Washington County Mental Health Association; Dr. Frank J. Ayd, Jr., at the Holy Trinity Council KC; Dr. Neal Aronson at the Maryland Academy of Medicine and Surgery; Dr. Elizabeth Winiarz at St. Martin's Guild; Dr. S. Ralph Andrews, Elkton, at the Kenmore PTA; and Dr. Richard W. TeLinde at the Goucher Club.

EUROPEAN TOUR

The Faculty is sponsoring a European Tour for its members, immediate family, and friends. Departure will be July 15 by JET (Boeing 707) to London, England (where a Joint Clinical Session with the British Medical Association will be held on July 18) and return passage - when you desire. If you are interested, please complete the blank shown below. (See Page 644 for further details.)

Two separate tour arrangements will be available for this trip. Escorted and individual tours are available. Escorted tour prices include: air and rail transportation in Europe, first class hotel accommodations, meals, sight-seeing tours, and transfers to and from hotels. Individual tours are available at a fractional amount more than the escorted tours listed.

Escorted Tours. (Please list the tour in which you are interested.)

1. Middle Europe. ☐
2. Mediterranean. ☐
3. Scandinavian Countries ☐

If individual specialized tour desired, check here. ☐

If individual tour desired, list countries you wish to visit._____

"CHIROPRACTIC PHYSICIAN" USE ILLEGAL

The use of the term "Chiropractic Physician" is illegal according to a recent ruling received from the State La Department. Any violations of this law should be reported to the Medical and Chirurgical Faculty for further action.

MORE SPEAKERS

Dr. Sidney Scherlis at the American Heart Association; Dr. Sibyl Mandell at the William Paca School PTA; Dr. Victor A. McKusick at the American Heart Association; and Dr. Lawrence S. Kubie at the Maryland Psychiatric Society.

CARROLL COUNTY HOSPITAL

Groundbreaking ceremonies for the Carroll County General Hospital were held on November 1, at the site on Gist Road.

REGIONAL AGING MEETINGS

The Governor's Commission on the Aging is scheduling various regional state meetings to discuss all phases of the Aging problems. A partial list, subject to change, of these meetings is as follows:

January 20, 1960, Laurel Children's Center, all day
March, 1960, Eastern Shore, including Cecil County
April, 1960, Western Maryland

Other meetings planned, but not set as far as date is concerned are for Baltimore area, including Anne Arundel Carroll, Harford, Baltimore and Howard Counties; and a meeting for the Prince George's and Montgomery County area.

OFFICE ASSISTANT PLANS

Regional meetings for Doctor's Office Assistants are planned for early in 1960. The first will include Prince George's, Anne Arundel, Montgomery and other contiguous counties. Full details will be given at a later date.

John Sargeant
Executive Secretary

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Caffeine ..... gr. ½
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...providing the desired gradation of potencies for relief of varying intensities of pain

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simple headache
rheumatic conditions
arthralgias
myalgias
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earache
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neuralgia
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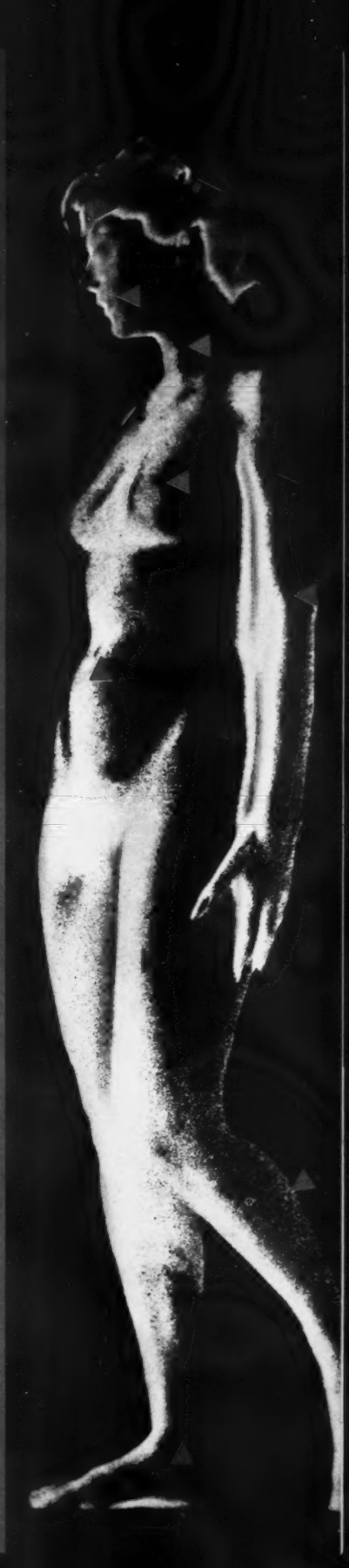
premenstrual tension
minor surgery
post-partum pain
trauma
organic disease
neoplasm
muscle spasm
colic
migraine
musculo-skeletal pains
postdental surgery
post-partum involution
fractures
synovitis/bursitis

relief of pain
of all degrees of
severity up to
that which
requires morphine

AND IN
fevers
dry,
unproductive coughs



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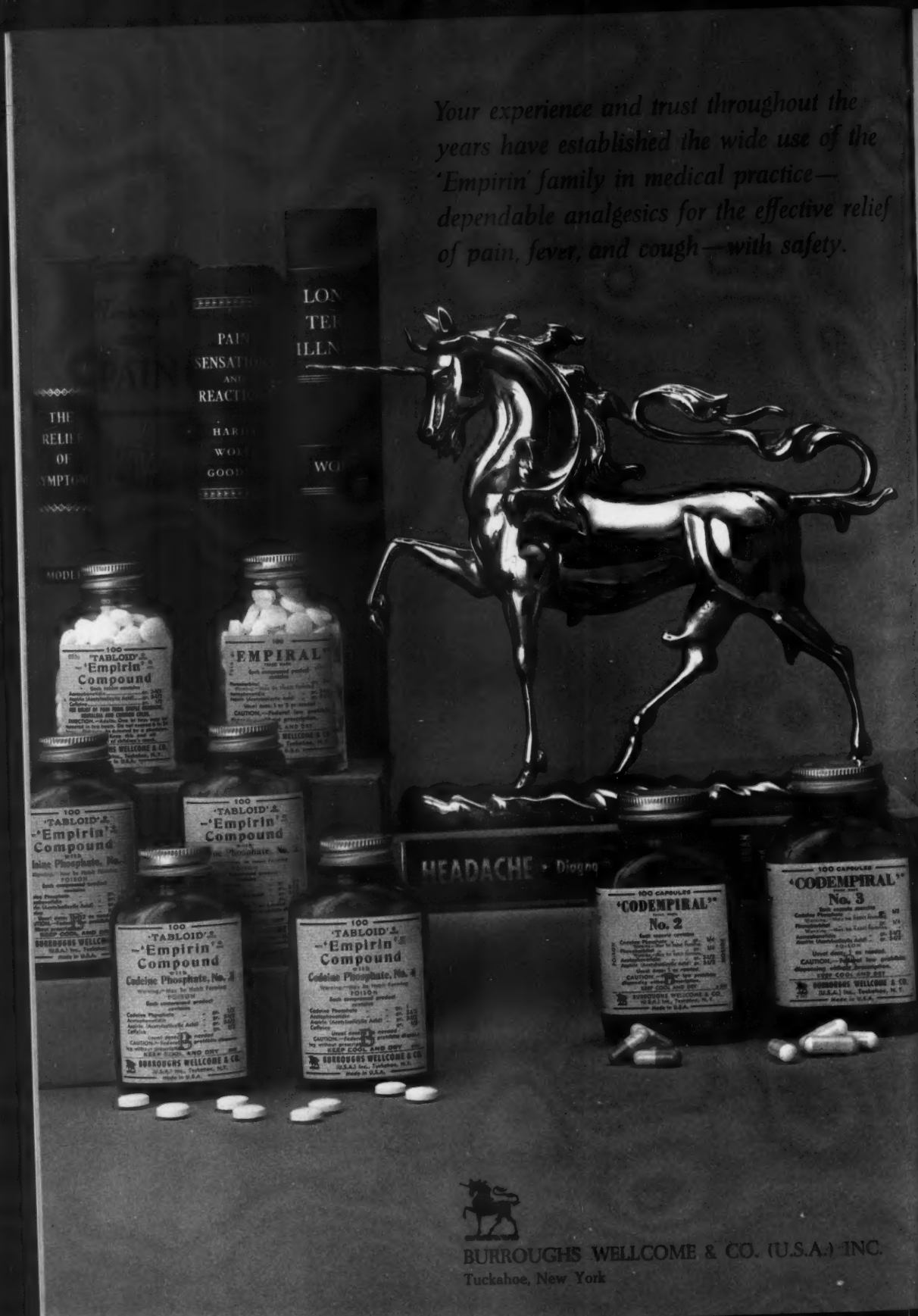
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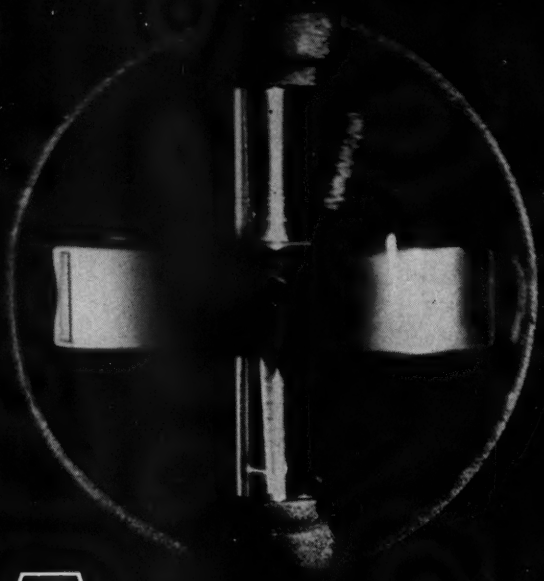
minimal disturbance
of the patient's chemical and psychic balance...



still unsurpassed for total corticosteroid benefits

Arist

Substantiated by published reports of leading clinicians:

- **effective control** of allergic and inflammatory symptoms[1-20]
- **minimal disturbance** of the patient's chemical and psychic balance[1, 4, 5, 8-19]

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stocort®

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nti-inflammatory and antiallergic levels ARISTOCORT means:

- **freedom from salt and water retention**
- **virtual freedom from potassium depletion**
- **negligible calcium depletion**
- **euphoria and depression rare**
- **no voracious appetite—no excessive weight gain**
- **low incidence of peptic ulcer**
- **low incidence of osteoporosis with compression fracture**

dications: rheumatoid arthritis; arthritis; respiratory allergies; allergic and inflammatory rmatoses; disseminated lupus erythematosus; nephrotic syndrome; lymphomas and leukemias.
ecautions: With ARISTOCORT all traditional precautions to corticosteroid therapy should be ob-ed. Dosage should always be carefully adjusted to the smallest amount which will suppress mptoms. After patients have been on steroids for prolonged periods, discontinuance must be rried out gradually.
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References: 1. Feinberg, S.M., Feinberg, A.R., and Fisherman, E.W.: *J.A.M.A.* 167:58 (May 3) 1958. 2. Epstein, J.I. and Sherwood, H.: *Connecticut Med.* 22:822 (Dec.) 1958. 3. Friedlaender, S. and Friedlaender, A.S.: *Antibiotic Med. & Clin. Ther.* 5:315 (May) 1958. 4. Segal, M.S. and Duvenci, J.: *Bull. Tufts North East M. Center* 4:71 (April-June) 1958. 5. Segal, M.S.: Report to the A.M.A. Council on Drugs, *J.A.M.A.* 169:1063 (March 7) 1958. 6. Sherwood, H. and Cooke, R.A.: *J. Allergy* 28:97 (Mar.) 1958. 7. Duke, C.J. and Oviedo, R.: *Antibiotic Med. & Clin. Ther.* 5:710 (Dec.) 1958. 8. McGavack, T.H.: *Clin. Med.* (June) 1958. 9. Freyberg, R.H.; Berntsen, C.A., and Hellman, L.: *Arthritis and Rheumatism* 1:215 (June) 1958. 10. Hartung, E.F.: *J.A.M.A.* 167:973 (June 21) 1958. 11. Hartung, E.F.: *J. Florida Acad. Gen. Pract.* 8:18, 1958. 12. Zuckner, J.; Ramsey, R.H.; Caciolo, C., and Gantner, G.E.: *Ann. Rheum. Dis.* 17:398 (Dec.) 1958. 13. Appel, B.; Tye, M.J., and Leibsohn, E.: *Antibiotic Med. & Clin. Ther.* 5:716 (Dec.) 1958. 14. Kalz, F.: *Canad. M.A.J.* 79:400 (Sept.) 1958. 15. Mullins, J.F., and Wilson, C.J.: *Texas State J. Med.* 54:648 (Sept.) 1958. 16. Shelley, W.B.; Harun, J.S., and Pillsbury, D.M.: *J.A.M.A.* 167:959 (June 21) 1958. 17. DuBois, E.F.: *J.A.M.A.* 167:1590 (July 26) 1958. 18. McGavack, T.H.; Kao, K.T.; Leake, D.A.; Bauer, H.C., and Berger, H.E.: *Am. J. Med. Sc.* 236:720 (Dec.) 1958. 19. Council on Drugs: *J.A.M.A.* 169:257 (Jan. 17) 1959. 20. Rein, C.R.; Fleischmajer, R., and Rosenthal, A.R.: *J.A.M.A.* 165:1821 (Dec. 7) 1957.

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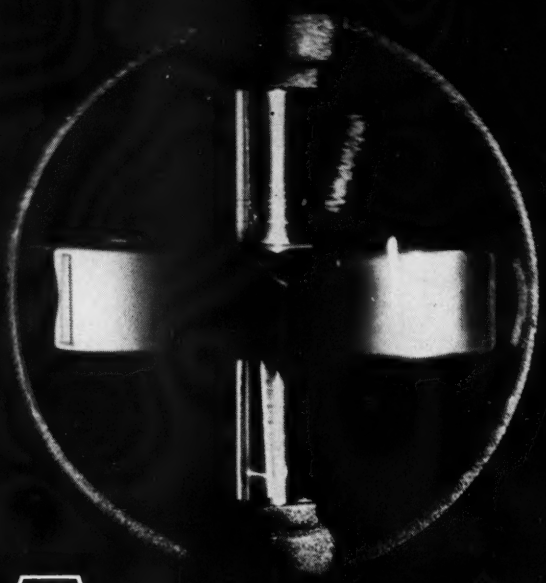

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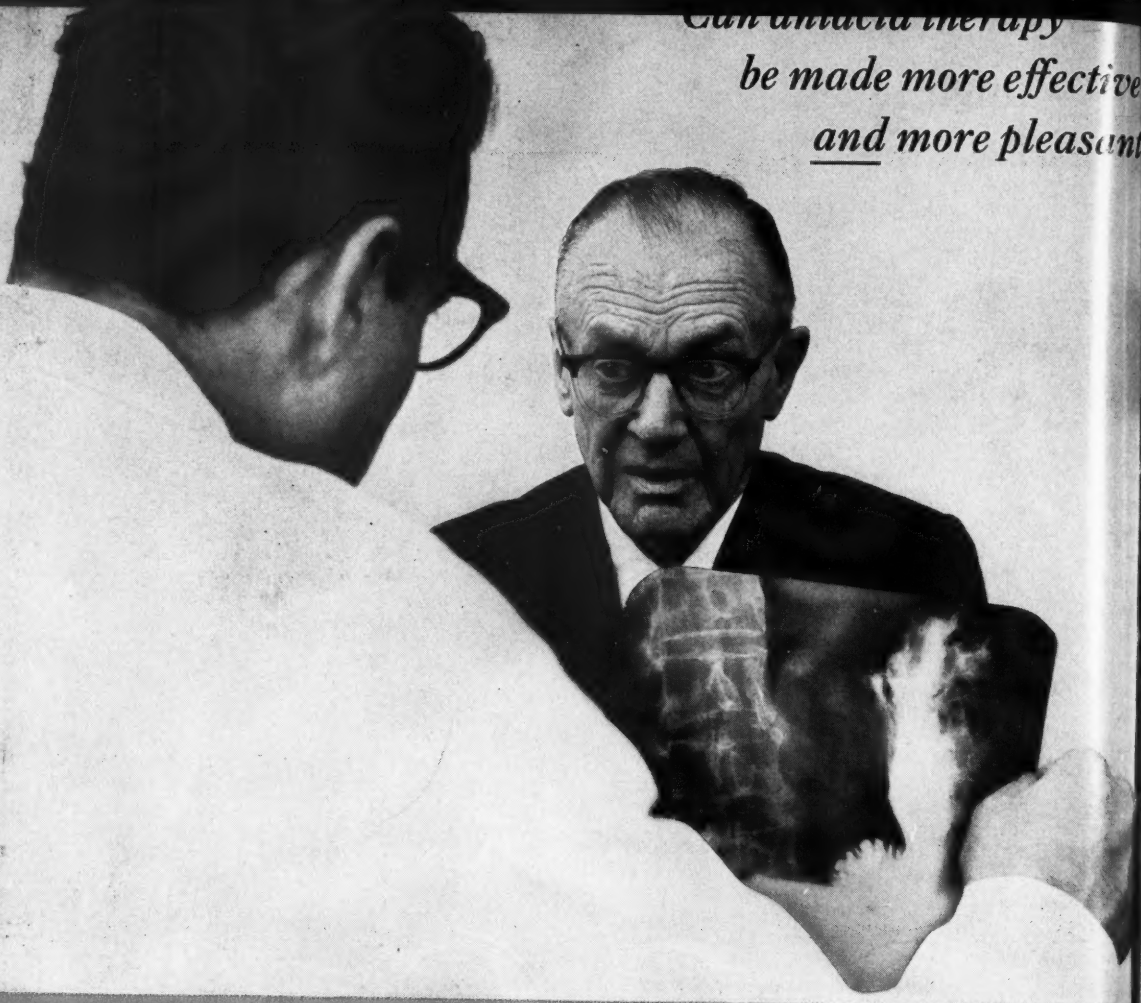

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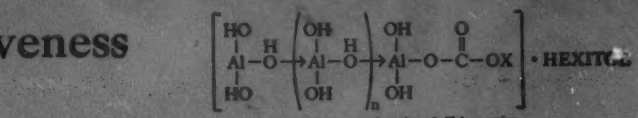
5. *More pleasant to take*

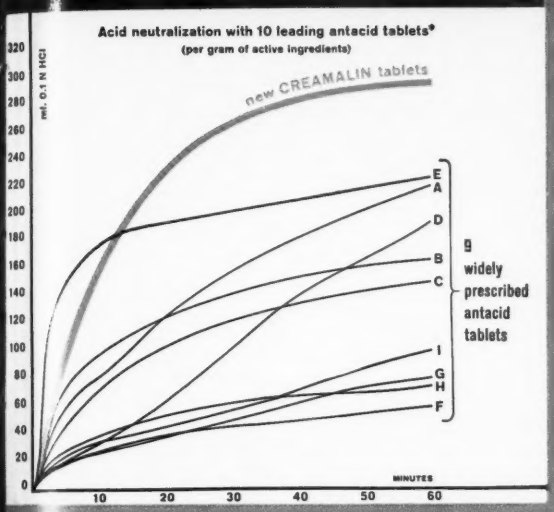
a new high in effectiveness and palatability



n is at least 1 and averages less than 6. X is a cation.

CREAMALIN NEUTRALIZES *MORE* ACID *FASTER*

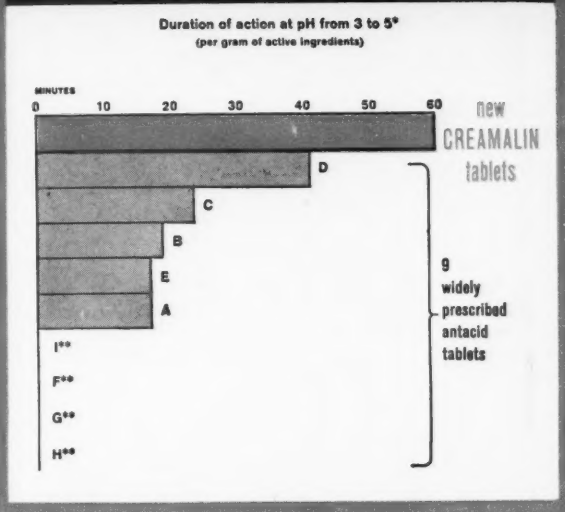
Quicker Relief • Greater Relief



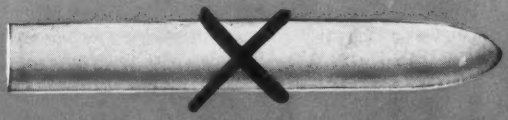
Tablets were powdered and suspended in distilled water in a constant temperature container (37°C) equipped with mechanical stirrer and pH electrodes. Hydrochloric acid was added as needed to maintain pH at 3.5. Volume of acid required was recorded at frequent intervals for one hour.

CREAMALIN NEUTRALIZES *MORE* ACID *LONGER*

More Lasting Relief



*Hinkel, E. T., Jr., Fisher, M. P. and Tainter, M. L.: A new highly reactive aluminum hydroxide complex for gastric hyperacidity. To be published.
**pH stayed below 3.



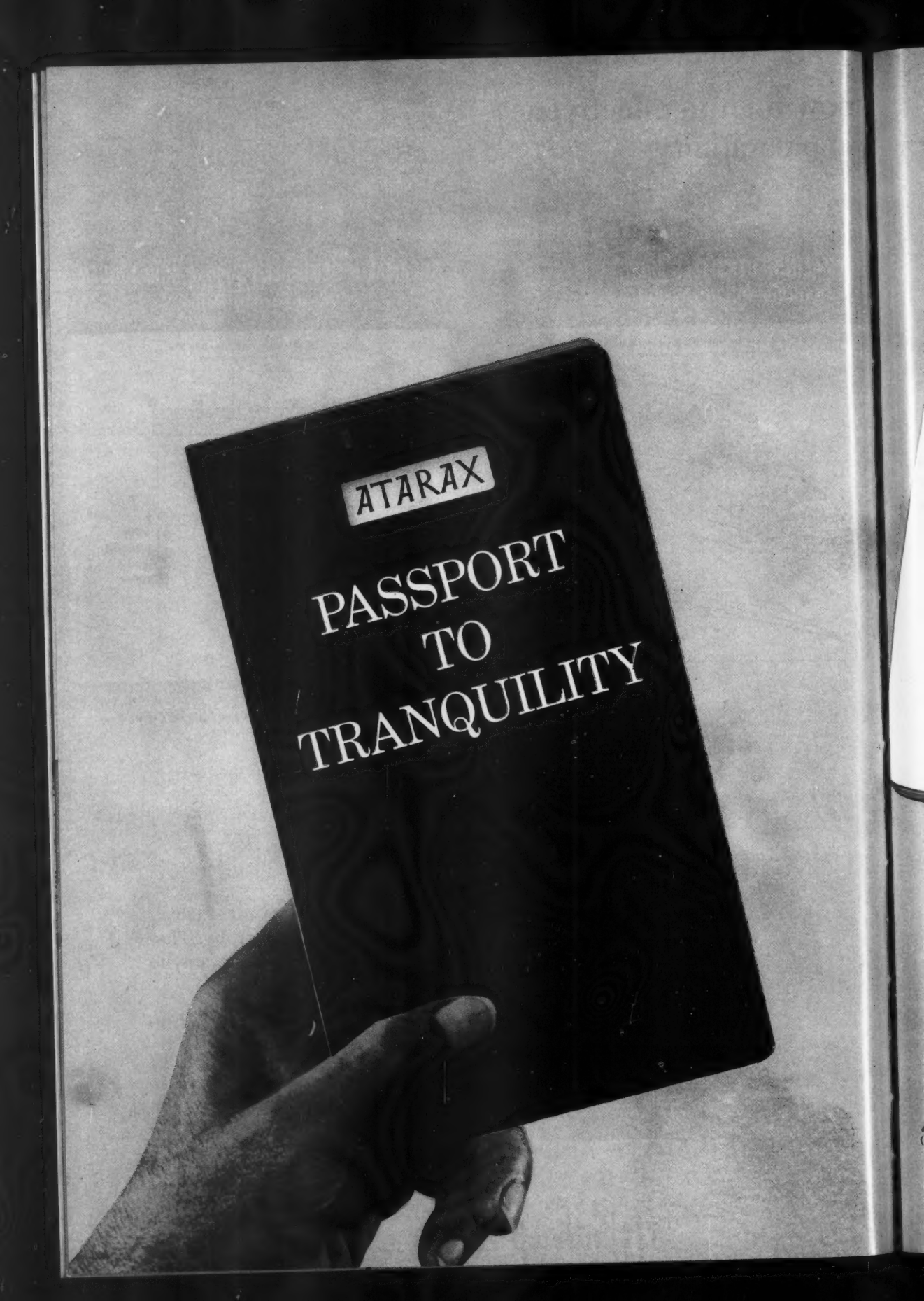
No chalky taste. New CREAMALIN tablets are not chalky, gritty, rough or dry. They are highly palatable, soft, smooth, easy to chew, mint flavored.

• NO ACID REBOUND • NO CONSTIPATION
• NO SYSTEMIC EFFECT

Adult Dosage: Gastric hyperacidity: 2 to 4 tablets as necessary. Peptic ulcer or gastritis: 2 to 4 tablets every two to four hours. Tablets may be chewed, swallowed with water or milk, or allowed to dissolve in the mouth.

Supplied: Bottles of 50, 100, 200 and 1000.

Winthrop LABORATORIES • NEW YORK 18, NEW YORK


ATARAX
PASSPORT
TO
TRANQUILITY

Passport

☞ **a universal record of effectiveness**

In anxiety, tension and agitation, ATARAX "... produced a more favorable state of calm and tranquility than any drug previously used."[1]

☞ **widest latitude of safety and flexibility**

No serious adverse reaction ever documented – five dosage forms and sizes

☞ **chemically distinct among tranquilizers**

Not a phenothiazine or a meprobamate

☞ **added frontiers of usefulness**

These unique benefits in specific indications

ANTIHISTAMINIC
ANTIARRHYTHMIC
ANTISECRETORY

BACKED BY A WORLD OF EXPERIENCE

Dosage: ADULTS, one 25 mg. tablet, or one tbsp. Syrup q.i.d. CHILDREN – 3-6 years, one 10 mg. tablet or one tsp. Syrup t.i.d.; over 6 years, two 10 mg. tablets or two tsp. Syrup t.i.d.

Supplied: Tiny 10 mg., 25 mg., and 100 mg. tablets, bottles of 100. Syrup, pint bottles. Parenteral Solution, 10 cc. multiple-dose vials.

References: 1. Farah, L.: Internat. Rec. Med. *169*:379 (June) 1956. 2. Smigel, J. O., et al.: J. Am. Geriatrics Soc. *7*:61 (Jan.) 1959. 3. Feinberg, A. R., et al.: J. Allergy *29*:358 (July) 1958. 4. Eisenberg, B. C.: J.A.M.A. *169*:14 (Jan. 3) 1959. 5. Maryssael, L.: Bruxelles-méd. *38*:141 (Jan. 26) 1958. 6. Pfleger, R.: Med. Klin. *53*:1030 (June 5) 1958. 7. Over 200 laboratory and clinical papers from 14 countries.

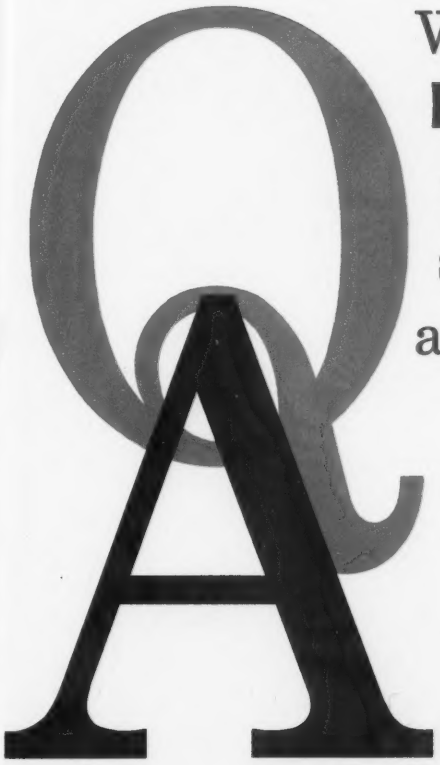
ATARAX®

PASSPORT TO TRANQUILITY

(brand of hydroxyzine)

Rx PFIZER

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being



Why should I use KANTREX® Injection* when there are so many other antibiotics available?

Because KANTREX Injection is bactericidal to a wide variety of organisms, including many that are highly resistant to the other antibiotics[3,4,10,12,13,17,18,20,21,23,24,25,27,30,33,35,37]

—organisms such as *Staph. aureus, Staph. albus, A. aerogenes, E. coli, H. pertussis, K. pneumoniae, Neisseria* sp., *Shigella, Salmonella* and many strains of *B. proteus.*

Q *But if I use* KANTREX *Injection, won't that help make bacteria resistant to it also?*

Next page, please .....

* Kanamycin sulfate injection (Bristol)

Q *But if I use* KANTREX *Injection, won't that help make bacteria resistant to it also?*

A A very good question, but it is reassuring to note that in almost two years of clinical use of KANTREX for the treatment of infections for which it is recommended, the emergence of KANTREX-resistant bacterial populations has not been a problem.

Q *My impression is that* KANTREX *is just another neomycin. Isn't that so?*

A Indeed not. The only thing KANTREX and neomycin have in common is a similar antimicrobial spectrum. Otherwise, they're very different: they have different chemical structures; the toxicity of KANTREX is "much less than that of neomycin"[14]; and clinically, KANTREX Injection is practical for systemic administration routinely, while neomycin is not.

Q *You mean that* KANTREX *Injection doesn't have the nephrotoxicity of neomycin?*

A Precisely. It's true that when KANTREX Injection is used, urinary casts – even slight albuminuria or microscopic hematuria – may appear, especially in poorly hydrated patients, but this does not reflect any progressive damage to the kidneys. These signs promptly disappear on adequate hydration or termination of therapy.

Q *Then why do you recommend reduced dosage in patients with renal impairment?*

A Because renal impairment causes an excessive accumulation of KANTREX in the blood and tissues, when usual doses are administered. Since KANTREX Injection is excreted entirely by the kidneys, renal impairment leads

to unnecessarily high and prolonged blood levels; and such excessive concentrations increase the risk of ototoxicity.

Q *Is that why we see reports of patients developing hearing loss during* KANTREX *Injection therapy?*

A Yes. A study of the few reported cases in which patients have suffered impaired hearing will show that in every instance they had pre-existing or concurrent renal impairment, yet received usual or excessive doses of KANTREX Injection. Dosage recommendations for KANTREX Injection emphasize that in patients with renal dysfunction, adequate serum levels can be achieved with a fraction of the dose suggested for patients with normal kidney function – with minimal risk of ototoxicity.

Q *Since urinary tract infections are often accompanied by renal impairment, does that mean I shouldn't use* KANTREX *Injection in such conditions?*

A Not at all. With proper precautions, KANTREX Injection is an excellent drug for the treatment of urinary tract infections, especially those due to *Proteus, A. aerogenes* and *E. coli*, even when renal impairment is present.

Q *What are the "proper precautions" in a patient with impaired renal function?*

A The package literature covers them in detail. First, the daily dose should be reduced in such a patient. Then, if he is going to receive KANTREX Injection for 7 days or more, a pre-treatment audiogram should be done, and it should be repeated at appropriate intervals during therapy. If tinnitus or subjective hearing loss develops, or if followup audiograms show significant loss of high frequency response, KANTREX therapy should be discontinued. However, therapy for 7 days or more

is seldom required because the clinical response to KANTREX Injection is so rapid.

Q *Why do you put so much emphasis on* KANTREX'S *"rapid action"? Every antibiotic I've heard about is supposed to be "rapid acting."*

A There is such an abundance of clinical evidence about "rapid acting" that it takes KANTREX Injection out of the "supposed-to" class.[1,2,3,7,8,9,11,15,16,19,21,22,26,29,32,33] Remember, the effectiveness of KANTREX Injection therapy can usually be appraised in 24 to 36 hours. That's definite evidence of rapid action. In fact, one group of investigators reported that "the rapidity with which bacteria are killed by this agent is reflected by the promptness of the clinical response."[29]

Q *Does* KANTREX *Injection cause blood dyscrasias?*

A In extensive clinical and toxicity studies by numerous investigators, as well as almost two years of general use, not a single instance of such toxicity has been reported.

Q *Can I administer* KANTREX *Injection in any other way than by the intramuscular route?*

A Yes. While it's usually given intramuscularly, other routes are practicable: intravenous, intraperitoneal, by aerosol, and as an irrigating solution. Complete instructions are included in the package insert.

Q *So you think I ought to use* KANTREX *Injection as my first choice antibiotic in staph and gram-negative infections?*

A Yes – because all evidence to date indicates that it is bactericidal against a wide range of organisms... rapid acting... does not encourage development of bacterial resistance... is well tolerated in specified dosage... and has not caused any blood dyscrasias.

KANTREX® CAPSULES

for local gastrointestinal therapy... not for systemic infections

Q *Why can't I use* KANTREX *Capsules for systemic medication?*

A Because there is only negligible absorption of KANTREX from the gastrointestinal tract.[3,5,6,8,28,34] Thus, capsules cannot provide effective blood levels.

Q *Then what are* KANTREX *Capsules used for?*

A Preoperative bowel sterilization, and local treatment of intestinal infections due to kanamycin-sensitive organisms.

Q *I've been using neomycin for preoperative bowel sterilization. Why should I switch to* KANTREX *Capsules?*

A Because KANTREX has been rated as "superior to neomycin" for this purpose.[6] It provides rapid and satisfactory control of coliforms, clostridia, staphylococci and streptococci; yeasts do not proliferate; stool concentrations of the drug are exceptionally high; and nausea, vomiting or intestinal irritation have not been observed.[5,6]

Q *What advantages do* KANTREX *Capsules offer me in the treatment of intestinal infections?*

A A high degree of effectiveness against most of the pathogens responsible for such infections: *Salmonella, Shigella, Staph. aureus, E. coli* and *Endamoeba histolytica.* Moreover, their use has been "remarkably free of any side effects."[31]

KANTREX®

INJECTION KANAMYCIN SULFATE INJECTION

INDICATIONS

Infections due to kanamycin-sensitive organisms, particularly staph or "gram-negatives": genito-urinary infections; skin, soft tissue and post-surgical infections; respiratory tract infections; septicemia and bacteremia; osteomyelitis and periostitis.

DOSAGE: INTRAMUSCULAR ROUTE

Recommended daily dose is 15 mg. per kg. of body weight, in 2 to 4 divided doses.

For intramuscular administration, KANTREX Injection should be injected deeply into the upper outer quadrant of the gluteal muscle.

TOXICITY

When the recommended precautions are followed, the incidence of toxic reactions to KANTREX is low. In well hydrated patients under 45 years of age with normal kidney function, receiving a total dose of 20 Gm. or less of KANTREX, the risk of ototoxic reactions is negligible.

In patients with renal disease and impaired renal function, the daily dose of KANTREX should be reduced in proportion to the degree of impairment to avoid accumulation of the drug in serum and tissues, thus minimizing the possibility of ototoxicity. In such patients, if therapy is expected to last 7 days or more, audiograms should be obtained prior to and during treatment. KANTREX therapy should be stopped if tinnitus or subjective hearing loss develops, or if audiograms show significant loss of high frequency response.

OTHER ROUTES OF ADMINISTRATION

KANTREX should be used by intravenous infusion only when the intramuscular route is impracticable. KANTREX can also be employed for intraperitoneal use, aerosol treatment, and as an irrigating solution. See package insert for directions.

PRECAUTIONS

Use of antibiotics may occasionally result in overgrowth of non-sensitive organisms. If superinfection appears during therapy, appropriate measures should be taken.

SUPPLY

Available in rubber-capped vials as a ready-to-use sterile aqueous solution in two concentrations (stable at room temperature indefinitely):

KANTREX Injection, 0.5 Gm. kanamycin (as sulfate) in 2 ml. volume.
KANTREX Injection, 1.0 Gm. kanamycin (as sulfate) in 3 ml. volume.

CAPSULES (for local gastrointestinal therapy; not for systemic medication)

INDICATIONS AND DOSAGE

For preoperative bowel sterilization: 1.0 Gm. (2 capsules) every hour for 4 hours, followed by 1.0 Gm. (2 capsules) every 6 hours for 36 to 72 hours.

For intestinal infections: Adults: 3.0 to 4.0 Gm. (6 to 8 capsules) per day in divided doses for 5 to 7 days. Infants and children: 50 mg. per kg. per day in 4 to 6 divided doses for 5 to 7 days.

PRECAUTION

Preoperative use of KANTREX Capsules is contraindicated in the presence of intestinal obstruction. Although only negligible amounts of KANTREX are absorbed through intact intestinal mucosa, the possibility of increased absorption from ulcerated or denuded areas should be considered.

SUPPLY

KANTREX Capsules, 0.5 Gm. kanamycin (as sulfate), bottles of 20 and 100.

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1. Andrieu, G., Monnier, J., and Bourse, R.: Presse Med. 67:718, 1959. 2. Berger, S. H., and Wehrle, P. F.: Ann. N. Y. Acad. Sci. 76:136, 1958. 3. Bunn, P. A., Baltch, A., and Krajnyak, O.: *Ibid.* 76:109, 1958. 4. Bunn, P. A., and Baltch, A.: New Eng. J. Med. 259:659, 1958. 5. Cohn, I., Jr., and Longacre, A. B.: S. G. & O. 108:100, 1959. 6. Cohn, I., Jr.: Ann. N. Y. Acad. Sci. 76:212, 1958. 7. Cronk, G. A., and Naumann, D. E.: *Ibid.* 76:308, 1958. 8. Cronk, G. A., and Naumann, D. E.: J. Lab. & Clin. Med. 53:888, 1959. 9. Davies, F. G.: Ann. N. Y. Acad. Sci. 76:129, 1958. 10. Dougherty, L. J., Seneca, H., and Lattimer, J. K.: Antibiotics Annual 1958-1959, p. 713. 11. Dube, A. H.: Am. Pract. & Digest Treat. 10:1165, 1959. 12. Finegold, S. M., *et al.*: Antibiotics Annual 1958-1959, p. 606. 13. Finegold, S. M., *et al.*: Ann. N. Y. Acad. Sci. 76:319, 1958. 14. Finland, M.: *Ibid.* 76:391, 1958. 15. Finland, M.: Lancet 2:209, 1958. 16. Fujii, R., *et al.*: J. Japan M. A. 39:740, 1958; abst. World-Wide Abst. Gen. Med. 2:28, 1959. 17. Gourevitch, A., Hunt, G. A., and Lein, J.: Ant. & Chemo. 8:149, 1958. 18. Gourevitch, A., *et al.*: Ann. N. Y. Acad. Sci. 76:31, 1958. 19. Greey, P. H., and Wightman, K. J. R.: *Ibid.* 76:224, 1958. 20. Griffith, L. J., and Ostrander, W. E.: Ant. & Chemo. 9:416, 1959. 21. Hewitt, W. L., and Finegold, S. M.: Ann. N. Y. Acad. Sci. 76:122, 1958. 22. High, R. H., Sarria, A., and Huang, N. N.: *Ibid.* 76:289, 1958. 23. Hirsh, H. L.: Sibley Mem. Hosp. Alumni Assn. Bull. 2:16, 1959. 24. Hunt, G. A., and Moses, A. J.: Ann. N. Y. Acad. Sci. 76:81, 1958. 25. Lattimer, J. K., Seneca, H., Zinsser, H. H. and Troc, O.: J.A.M.A. 170:938, 1959. 26. Prigot, A., Shidlovsky, B. A., and Campbell, E. A.: Ann. N. Y. Acad. Sci. 76:204, 1958. 27. Riley, H. D., Jr.: Antibiotics Annual 1958-1959, p. 623. 28. Ruiz Sanchez, F., *et al.*: *Ibid.*, p. 725. 29. Rutenburg, A. M., Koota, G. M., and Schweinburg, F. B.: Ann. N. Y. Acad. Sci. 76:348, 1958. 30. Slotkin, E. A.: Postgrad. Med. 25:433, 1959. 31. Thurman, W. G., and Platou, R. V.: Ann. N. Y. Acad. Sci. 76:230, 1959. 32. Welch, H., *et al.*: *Ibid.* 76:66, 1958. 33. White, A., and Knight, V.: *Ibid.* 76:277, 1958. 34. Yow, E. M.: Practitioner. 182:759, 1959. 35. Yow, E. M., *et al.*: A.M.A. Arch. Int. Med. 102:948, 1958. 36. Yow, M. D., Desmond, M. M., and Nickey, L. N.: J. Ped. 54:409, 1959. 37. Yow, M. D., and Womack, G. K.: Ann. N. Y. Acad. Sci. 76:363, 1958.

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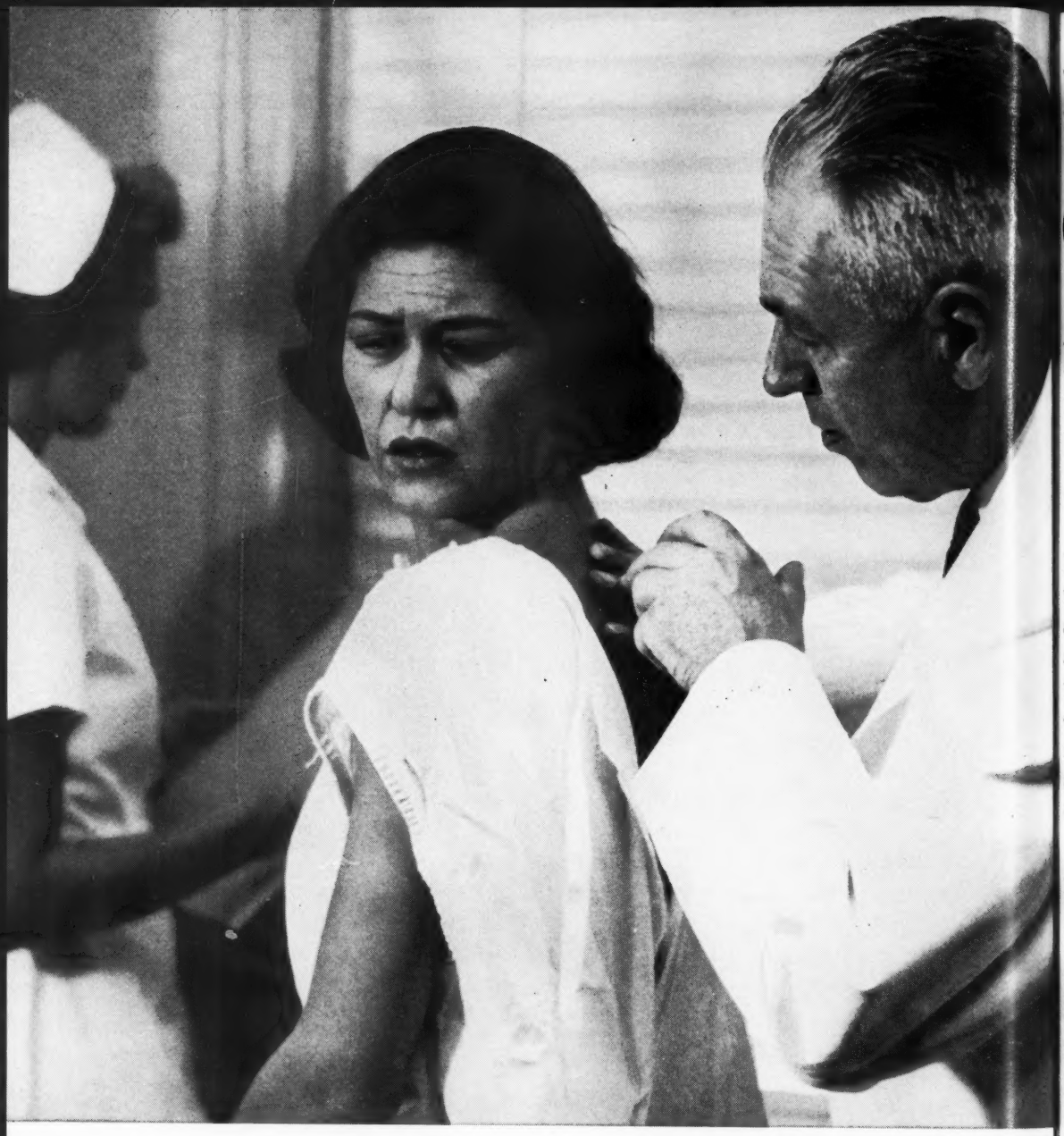

"I feel tired even after a full night's sleep."

Restores normal vitality in

emotional fatigue

Deprol relieves undue tiredness, apathy and depressed moods as it calms anxiety – without the risk of liver damage or extrapyramidal symptoms frequently reported with energizers or phenothiazines.

Emotional or nervous fatigue—undue tiredness, apathy, lethargy and listlessness—cuts sharply into the patient's usual physical and mental productivity. It is one of the most common conditions seen in every medical practice. Untreated, emotional fatigue may mushroom into a depressive episode, anxiety state, chronic fatigue or a mixture of these disorders.

Deprol acts fast to relieve emotional fatigue. It overcomes tiredness and lethargy, apathy and listlessness, thus restoring normal vitality and interest before the fatigue deepens. On Deprol, improvement is achieved without producing liver toxicity, hypotension, psychotic reactions, changes in sexual function or Parkinson-like reactions associated with energizers or phenothiazines.

BIBLIOGRAPHY (10 clinical studies, 714 patients):

1. Alexander, L. (35 patients): Chemotherapy of depression—Use of meprobamate combined with benactyzine(2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A.166:1019, March 1, 1958. **2.** Bateman, J. C. and Carlton, H. N. (50 patients): Deprol as adjunctive therapy for patients with advanced cancer. Antibiotic Med.& Clin. Therapy. In press, 1959. **3.** Bell, J. L., Tauber, H., Santy, A. and Pulito, F. (77 patients): Treatment of depressive states in office practice. Dis. Nerv. System **20**:263, June 1959. **4.** Breitner, C. (31 patients): On mental depressions. Dis. Nerv. System **20**:142, (Section Two), May 1959. **5.** McClure, C. W., Papas, P. N., Speare, G. S., Palmer, E., Slattery, J. J., Konefal, S. H., Henken, B. S., Wood, C. A. and Ceresia, G. B. (128 patients): Treatment of depression—New technics and therapy. Am. Pract. & Digest Treat. **10**:1525, Sept. 1959. **6.** Pennington, V. M. (135 patients): Meprobamate-benactyzine (Deprol) in the treatment of chronic brain syndrome, schizophrenia and senility. J. Am. Geriatrics Soc. **7**:656, Aug. 1959. **7.** Rickels, K. and Ewing, J. H. (35 patients): Deprol in depressive conditions. Dis. Nerv. System **20**:364, (Section One), Aug. 1959. **8.** Ruchwarger, A. (87 patients): Use of Deprol (meprobamate combined with benactyzine hydrochloride) in the office treatment of depression. M. Ann. District of Columbia **28**:438, Aug. 1959. **9.** Settel, E. (52 patients): Treatment of depression in the elderly with a meprobamate-benactyzine hydrochloride combination. Antibiotic Med. & Clin. Therapy. In press, 1959. **10.** Splitter, S. R. (84 patients): The care of the anxious and the depressed. Submitted for publication, 1959.

and

11. Laughlin, H. P.: The Neuroses in Clinical Practice, Saunders, Philadelphia, 1956, pp. 448-481.

▲Deprol▲®

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this may be gradually increased up to 3 tablets q.i.d.
Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.
Supplied: Bottles of 50 light-pink, scored tablets.

CD-483

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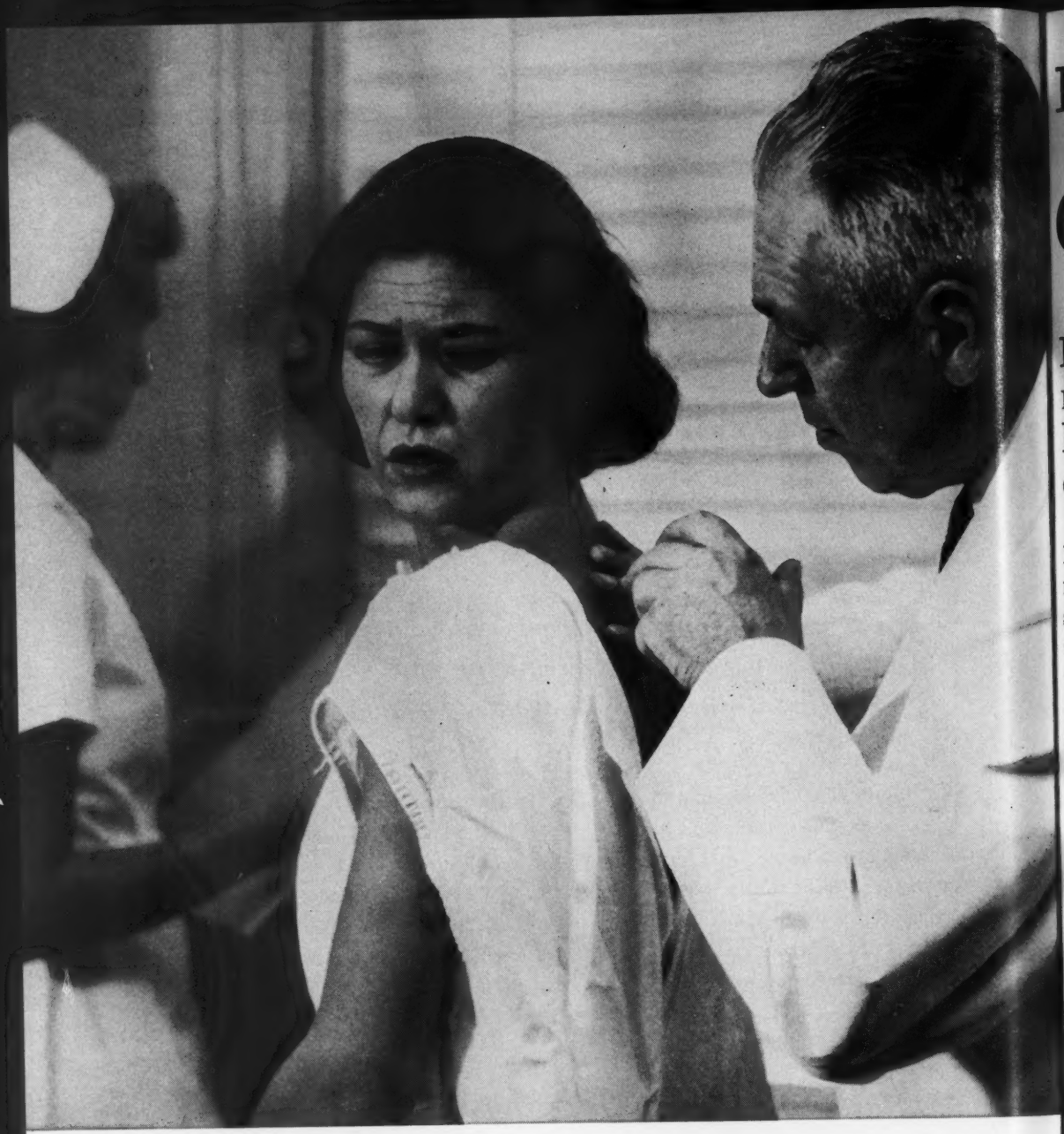

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Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.
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CD-482

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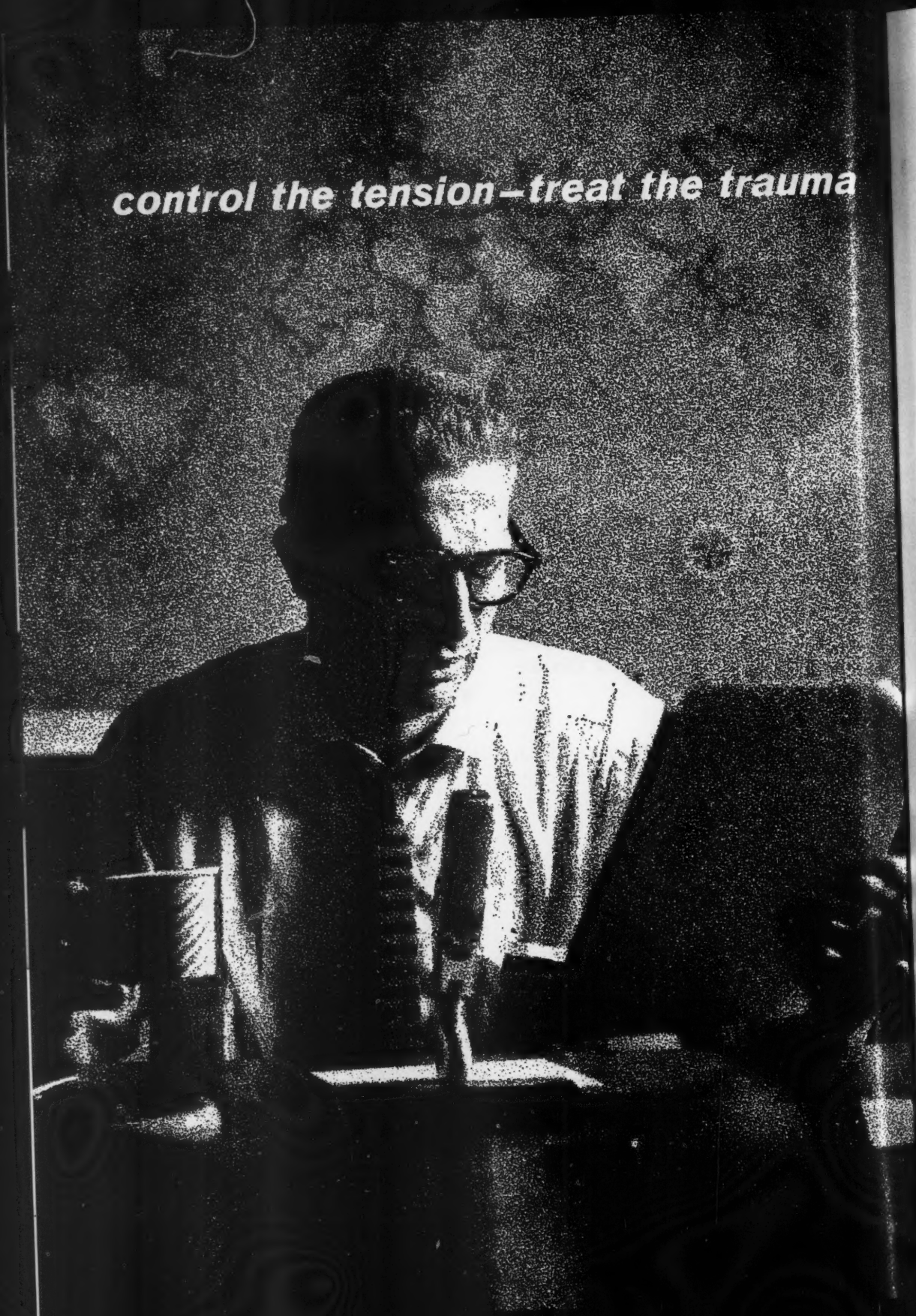

control the tension–treat the trauma

...Pathibamate® 400 200

meprobamate with PATHILON® tridihexethyl chloride Lederle

greater flexibility in the control of tension, hypermotility and excessive secretion in gastrointestinal dysfunctions

PATHIBAMATE combines two highly effective and well-tolerated therapeutic agents:

meprobamate (400 mg. or 200 mg.) widely accepted tranquilizer and...
PATHILON (25 mg.)—anticholinergic noted for its peripheral, atropine-like action, with few side effects.

The clinical advantages of PATHIBAMATE have been confirmed by nearly two years' experience in the treatment of duodenal ulcer; gastric ulcer; intestinal colic; spastic and irritable colon; ileitis; esophageal spasm; anxiety neurosis with gastrointestinal symptoms and gastric hypermotility.

Because of individual variation in the intensity of stimuli in gastrointestinal disorders, adequate dosage for optimum control may be expected to vary as well. The dosage strengths of PATHIBAMATE-400 and PATHIBAMATE-200 facilitate individualization of treatment in respect to both the degree of tension and associated G.I. sequelae, as well as the response of different patients to the component drugs.

Supplied: PATHIBAMATE-400—Each tablet (yellow, 1/2-scored) contains meprobamate, 400 mg.; PATHILON tridihexethyl chloride, 25 mg.
PATHIBAMATE-200—Each tablet (yellow, coated) contains meprobamate, 200 mg.; PATHILON tridihexethyl chloride, 25 mg.

Administration and Dosage: PATHIBAMATE-400—1 tablet three times a day at mealtime and 2 tablets at bedtime.
PATHIBAMATE-200—1 or 2 tablets three times a day at mealtime and 2 tablets at bedtime.
Adjust to patient response.

Contraindications: glaucoma; pyloric obstruction, and obstruction of the urinary bladder neck.

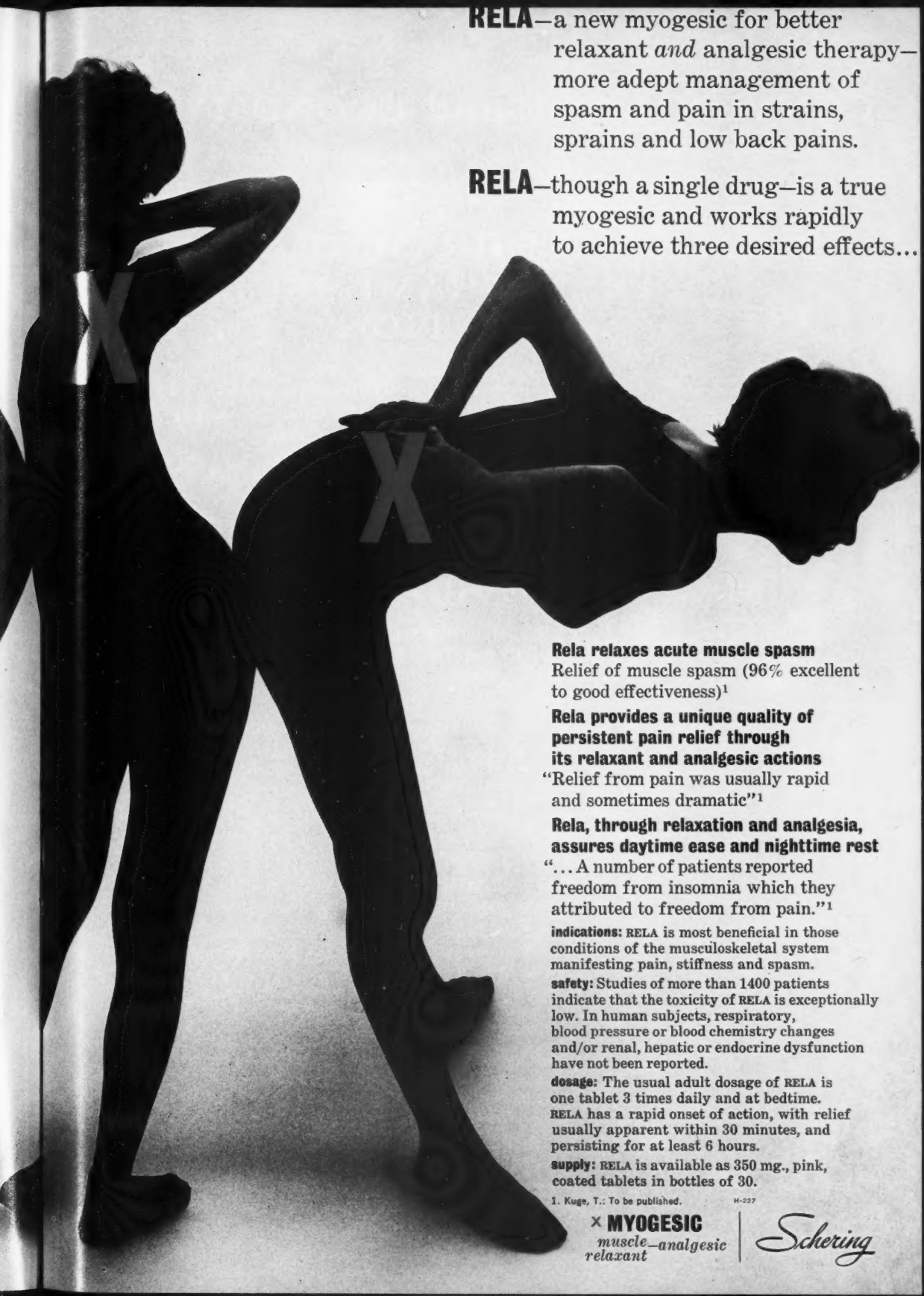
Lederle

LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

ANNOUNCING SCHERING'S NEW MYOGESIC[X]

RELA™ EASES STRAINS SPRAINS & LOW BACK PAINS...!

CARISOPRODOL



RELA—a new myogesic for better relaxant *and* analgesic therapy—more adept management of spasm and pain in strains, sprains and low back pains.

RELA—though a single drug—is a true myogesic and works rapidly to achieve three desired effects...

Rela relaxes acute muscle spasm
Relief of muscle spasm (96% excellent to good effectiveness)[1]

Rela provides a unique quality of persistent pain relief through its relaxant and analgesic actions
"Relief from pain was usually rapid and sometimes dramatic"[1]

Rela, through relaxation and analgesia, assures daytime ease and nighttime rest
"... A number of patients reported freedom from insomnia which they attributed to freedom from pain."[1]

indications: RELA is most beneficial in those conditions of the musculoskeletal system manifesting pain, stiffness and spasm.

safety: Studies of more than 1400 patients indicate that the toxicity of RELA is exceptionally low. In human subjects, respiratory, blood pressure or blood chemistry changes and/or renal, hepatic or endocrine dysfunction have not been reported.

dosage: The usual adult dosage of RELA is one tablet 3 times daily and at bedtime. RELA has a rapid onset of action, with relief usually apparent within 30 minutes, and persisting for at least 6 hours.

supply: RELA is available as 350 mg., pink, coated tablets in bottles of 30.

1. Kuge, T.: To be published.

H-227

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CAPSULES

Continuation with oral Cosa-Terramycin every six hours will provide highly effective antibacterial serum and tissue levels for prompt infection control.

The unsurpassed record of clinical effectiveness and safety established for Terramycin is your guide to successful antibiotic therapy.

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The authors' choice of dihydroxy aluminum aminoacetate (DAA) was based on the fact that "the tablet form of DAA (is) more active than a variety of straight aluminum hydroxide magmas." They further commented that "Because of the convenience of tablet medication as compared with the liquid gel—a convenience which in the use of other tablets is gained at the expense of therapeutic effectiveness—dihydroxy aluminum aminoacetate was used exclusively."

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The extended usefulness of TENTONE is readily apparent

TENTONE® Methoxypromazine Maleate is a new, distinctive phenothiazine... highly active ...for general use in mild and moderate emotional and psychosomatic disorders.

TENTONE elicits a striking, positive calming response[1,2]...with marked reduction of psychic disorientation, and low risk of blood, liver or other organic toxicity and intolerance.[1-4]

TENTONE parallels the weaker ataractics in low incidence of side effects. Freedom from induced depression is apparently even greater.[5]

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CONDITION	RHEUMATIC DISORDERS	ARTERIO-SCLEROSIS, MALIGNANCY	ALCOHOL-DRUG WITHDRAWAL

Dosage: Mild to moderate cases—average starting dose, one 10 mg. or one 25 mg. tablet three or four times daily. *Moderate to severe*—average starting dose, one 50 mg. tablet four times daily. *Supplied:* 10 mg., 25 mg., and 50 mg. tablets.

1. Bodi, T., and Levy, H.: Clinical report, cited with permission. 2. Wetzler, R. A., and Phillips, R. M.: Clinical report, cited with permission. 3. Prigot, A.: Clinical report, cited with permission. 4. Gosline, E., *et al.*: *Am. J. Psychiat.* 115:939 (April) 1959. 5. Turvey, S. E. C.: Clinical report, cited with permission.

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takes him off the tension treadmill

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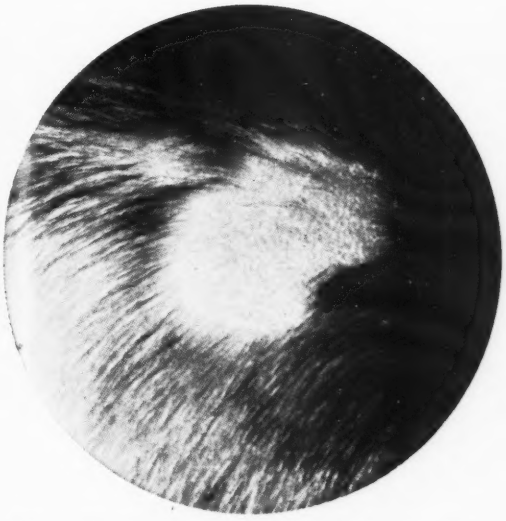
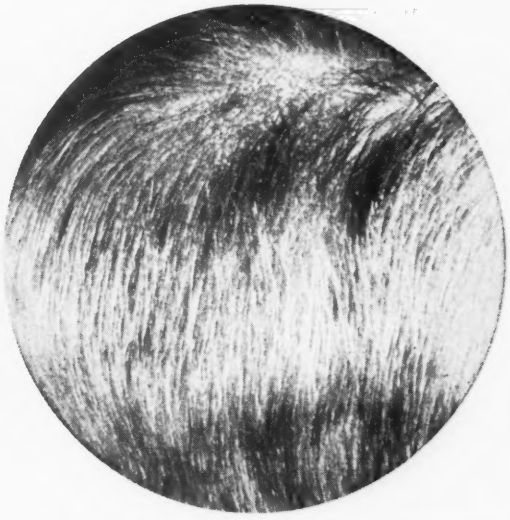
In tinea capitis



Before FULVICIN: Tinea capitis *(Microsporum audouini)* in a 7-year-old boy.



After FULVICIN: Normal, new hair growth after 6 weeks of oral therapy.

Photos courtesy of M. M. Nierman, M.D., Calumet City, Ill.

Lesions clear, cultures become negative in

tinea corporis: 4 to 5 weeks[1]
tinea cruris: 4 to 6 weeks[1]
onychomycosis: 4 to 6 months[1]
tinea pedis: 6 to 8 weeks[1]

first *oral* fungistat to penetrate keratin *from the inside*... acts to check invading ringworm fungi *(Microsporum, Trichophyton, Epidermophyton)*...usually well tolerated, side effects rare in therapeutic doses.

For complete information about dosage, indications and precautions consult Schering Statement of Directions.

Packaging: FULVICIN Tablets, 250 mg., bottles of 30 and 100.

1. Robinson, H. M., Jr., *et al.*: Griseofulvin, Clinical and Experimental Studies, A.M.A. Arch. Dermat., in press.

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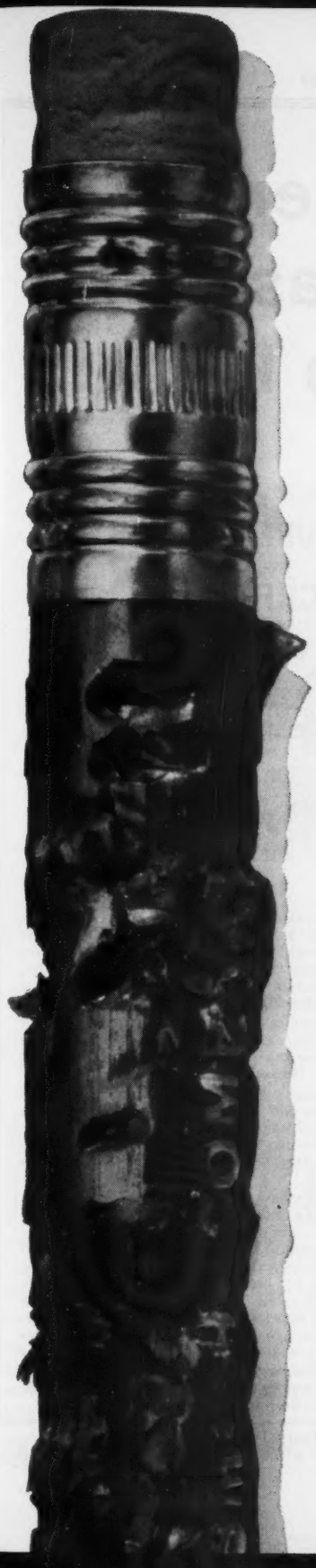


when you see signs of anxiety-tension specify

Dartal®

dihydrochloride

brand of thiopropazate dihydrochloride

for rapid relief of anxiety manifestations

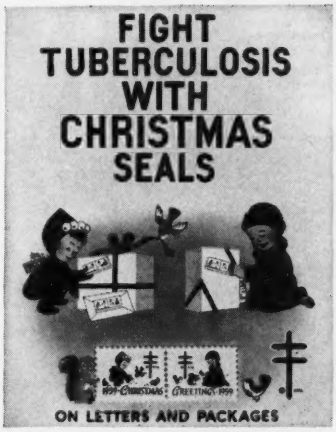
You will find Dartal outstandingly beneficial in management of the anxiety-tension states so frequent in hypertensive or menopausal patients. And Dartal is particularly useful in the treatment of anxiety associated with cardiovascular or gastrointestinal disease, or the tension experienced by the obese patient on restricted diet. You can expect consistent results with Dartal in general office practice.

with low dosage: Only one 2, 5 or 10 mg. tablet t.i.d. *with relative safety:* Evidence indicates Dartal is not icterogenic.

Clinical reports on Dartal: 1. Edisen, C. B., and Samuels, A. S.: A.M.A. Arch. Neurol. & Psychiat. *80*:481 (Oct.) 1958. 2. Ferrand, P. T.: Minnesota Med. *41*:853 (Dec.) 1958. 3. Mathews, F. P.: Am. J. Psychiat. *114*:1034 (May) 1958.

SEARLE

TB is not dead here . . . but Christmas Seals will help kill it!!!



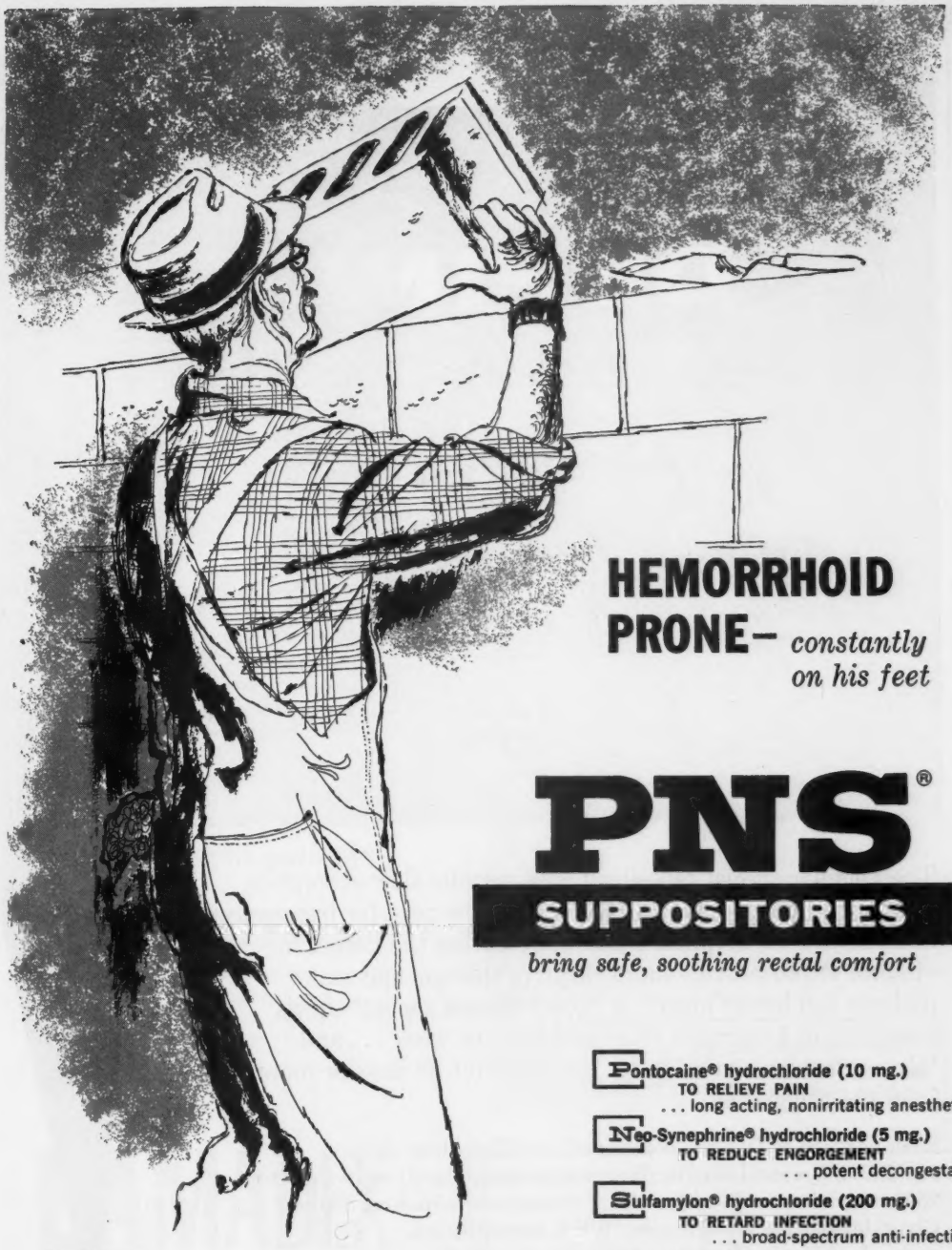
Last year, almost 2,000 *new*, active cases of tuberculosis were found in Maryland. Over 300 deaths in the state were caused by tuberculosis. There are still cases to be found and there are still people being treated whose cases were discovered previously. Surely, TB is not a dead disease.

TB is a communicable disease and anyone of us can catch it. Age, sex, race and occupation have nothing to do with it. *You* can catch TB. Don't say, "It can't happen to me" because it can.

Red Schoendienst, baseball star of the Milwaukee Braves, is some one who thought TB couldn't happen to him. But Red was wrong and last year he did catch TB. He's recovered now and has agreed to be the National Honorary Chairman for the 1959 Christmas Seal Sale.

Red learned the hard way what Christmas Seals are doing to get rid of tuberculosis. He learned that Christmas Seal funds are spent on chest X-rays and other casefinding programs, personal services to hospitalized patients, medical and scientific research and educational projects for professional TB workers, patients and the public alike. Your tuberculosis association hopes you will remember these things, too.

Christmas Seals have been an American tradition for more than fifty years. When you receive your Christmas Seal letter, please be generous. Keep the Christmas Seal tradition alive and help get rid of tuberculosis in Maryand. Buy—and use—Christmas Seals.



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Pontocaine® hydrochloride (10 mg.)
TO RELIEVE PAIN
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Directions:
1 suppository rectally after each bowel movement and on retiring.
How Supplied:
Boxes of 12.

As an added measure to promote rectal comfort while correcting bowel atonicity, add MUCILOSE®-SUPER to the patient's diet. This lubricating, nonirritating bulk laxative and stool softener will encourage easy, regular evacuation.

PNS, Pontocaine (brand of tetracaine), Neo-Synephrine (brand of phenylephrine), Sulfamylon (brand of mafenide) and Mucilose, trademarks reg. U. S. Pat. Off.

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greater specificity of tranquilizing action —divorced from such "diffuse" effects as anti-emetic action —explains why

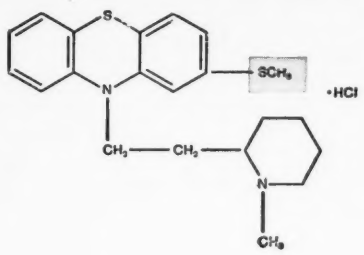
Mellaril®

THIORIDAZINE HCl

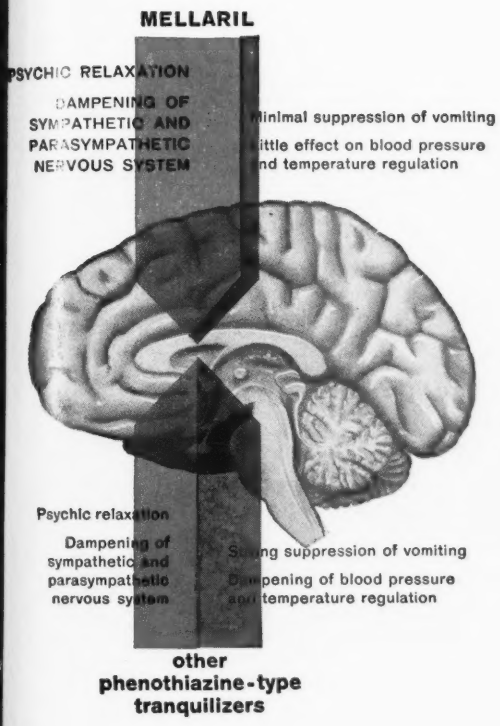
is virtually free of such toxic effects as jaundice · Parkinsonism · blood dyscrasia

"Thioridazine [MELLARIL] is as effective as the best available phenothiazine, but with appreciably less toxic effects than those demonstrated with other phenothiazines. . . . This drug appears to represent a major addition to the safe and effective treatment of a wide range of psychological disturbances seen daily in the clinics or by the general practitioner."*

a new advance in tranquilization:
greater specificity of tranquilizing action results in fewer side effects



The presence of a thiomethyl radical ($S\text{-}CH_3$) is unique in Mellaril and could be responsible for the relative absence of side effects and greater specificity of psychotherapeutic action. This is shown clinically by:



1 A specificity of action on certain brain sites in contrast to the more generalized or "diffuse" action of other phenothiazines. This is evidenced by a lack of appreciable anti-emetic effect.

2 Less "spill-over" action to other brain areas — hence, absence of undue sedation, drowsiness or autonomic nervous system disturbances.

3 A notable absence of extrapyramidal stimulation.

4 Lack of impairment of patient's normal drive and energy.

5 Virtual freedom from such toxic effects as jaundice, photosensitivity, skin eruptions, blood forming disorders.

INDICATION	USUAL STARTING DOSE	TOTAL DAILY DOSAGE RANGE
ADULTS: Mental and Emotional Disturbances:		
MILD—where anxiety, apprehension and tension are present	10 mg. t.i.d.	20-60 mg.
MODERATE—where agitation exists in psychoneuroses, alcoholism, intractable pain, senility, etc.	25 mg. t.i.d.	50-200 mg.
SEVERE—in agitated psychotic states as schizophrenia, manic depressive, toxic psychoses, etc.:		
Ambulatory	100 mg. t.i.d.	200-400 mg.
Hospitalized	100 mg. t.i.d.	200-800 mg.
CHILDREN: BEHAVIOR PROBLEMS IN CHILDREN	10 mg. t.i.d.	20-40 mg.

MELLARIL Tablets, 10 mg., 25 mg., 100 mg.

*Ostfeld, A. M.: Scientific Exhibit, American Academy of General Practice, San Francisco, April 6-9, 1959

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AN ANNOUNCEMENT
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FROM
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The first synthetic penicillin available for general clinical use

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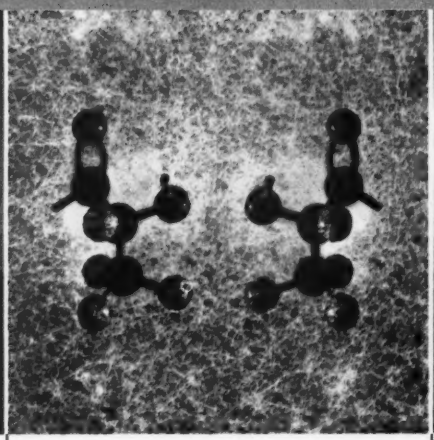
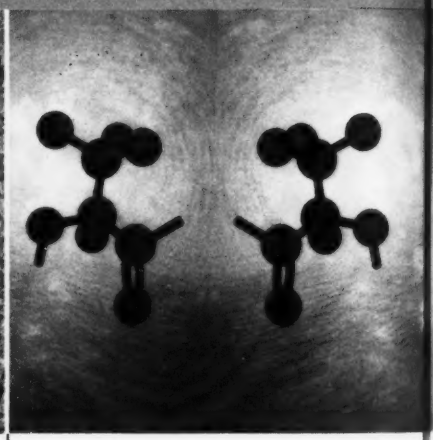




BLOOD LEVELS TWICE AS HIGH AS WITH POTASSIUM PENICILLIN V

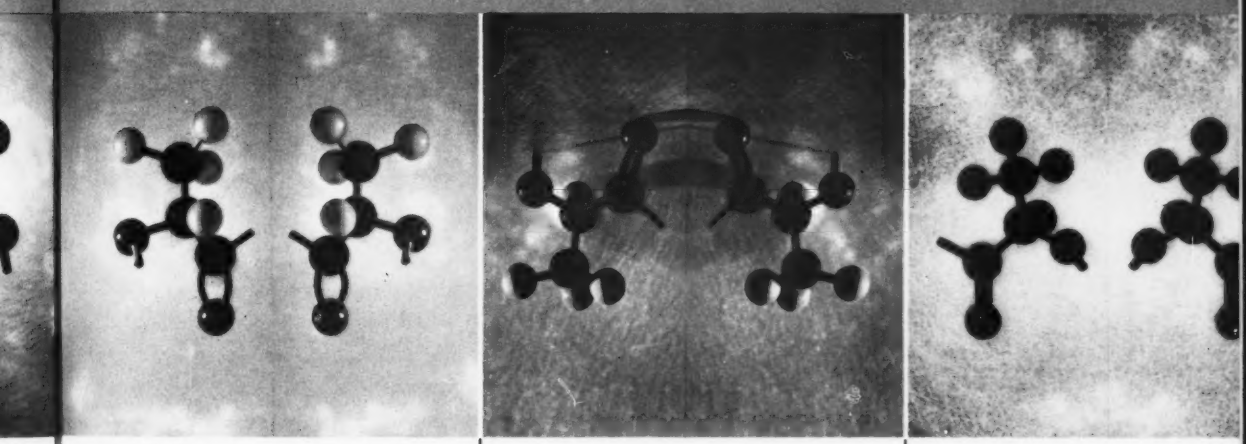
SAFER ORAL ROUTE PROVIDES HIGHER BLOOD LEVELS THAN INTRAMUSCULAR PENICILLIN G

IMPROVED ANTIBIOTIC EFFECT FROM COMPLEMENTARY ACTION OF ISOMERS

ADVANTAGES ACCOMPANY MOLECULAR ASYMMETRY

ILLIN

POTASSIUM PENICILLIN-152



ANTIBIOTIC ACTIVITY DIRECTLY PROPORTIONAL TO ORAL DOSE

REDUCED HAZARD OF SERIOUS ALLERGENICITY BY SAFER ORAL ROUTE

MANY STAPH STRAINS MORE SENSITIVE TO SYNCILLIN

BRISTOL

ORIGIN OF A NEW SYNTHETIC PENICILLIN

In March, 1957, Dr. John C. Sheehan of the Massachusetts Institute of Technology announced the total synthesis of penicillin from common raw materials, thus solving a problem which had baffled research workers for more than 15 years. Although total synthesis was not commercially practicable, this work, sponsored by Bristol Laboratories, made possible the subsequent synthesis of new penicillins not occurring in nature. Later scientists at Beecham Laboratories in England discovered that a key intermediate (6-aminopenicillanic acid) could be produced by a fermentation process. With these achievements, large scale production of synthetic penicillins became feasible.

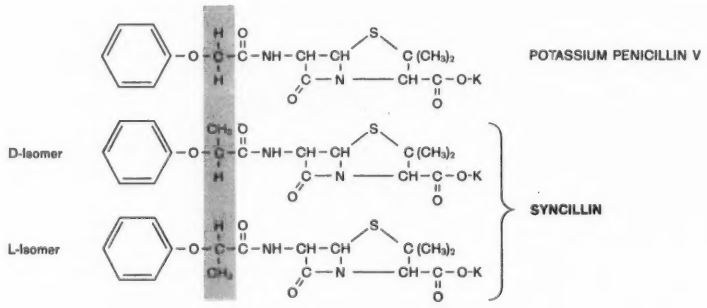
Organic chemists at Bristol then embarked upon an intensive program to develop better penicillins. Over five hundred were synthesized and underwent preliminary screening. Forty-six showed sufficient promise to warrant further investigation. Extensive microbiological, pharmacological, and clinical screening indicated that one compound, SYNCILLIN, had advantages of major importance over other penicillins.

SYNCILLIN is the N-acylation product of 6-aminopenicillanic acid and α-phenoxypropionic acid (the phenylether of lactic acid). It is freely soluble in water and remarkably resistant to decomposition by acid. The acid stability of SYNCILLIN is equivalent to that of penicillin V at pH 2 and pH 3 at 37° C.[1]

SIGNIFICANCE OF MOLECULAR ASYMMETRY AND ISOMERIC COMPLEMENTARITY

SYNCILLIN has a molecular configuration similar to penicillin V, but contains an additional CH_3 group so positioned as to render the adjacent carbon atom asymmetric. (In the formulae below, the added CH_3 group is shown in blue and the asymmetric carbon atom in red.) As a result, SYNCILLIN occurs as a mixture of two isomers.

Each isomer has been synthesized in essentially pure form and found to possess distinctive chemical and biological properties. The L-isomer is 2 to 17 times more active than the D-isomer against many of the organisms tested. As produced, SYNCILLIN is a mixture of the L-isomer and the D-isomer. As will be shown later, the antibiotic effect of the clinically available mixture, SYNCILLIN, is greater than either isomer alone against many organisms. This phenomenon is referred to here as *isomeric complementarity*.



SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

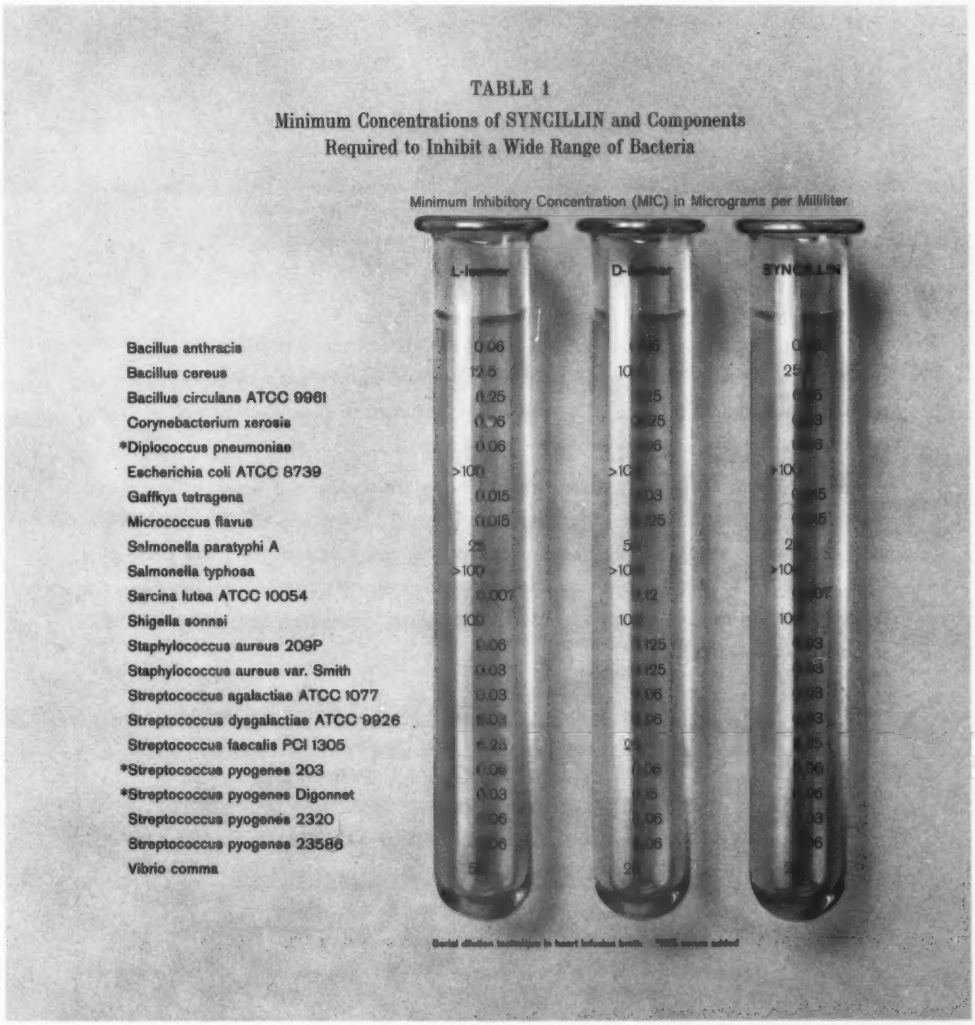
ISOMERIC COMPLEMENTARITY DEMONSTRATED IN VITRO

The *in vitro* minimum inhibitory concentration (MIC) of SYNCILLIN and of each of its two component isomers was determined for a variety of common pathogens and laboratory test organisms. As may be seen from Table 1, all three are highly effective against penicillin-susceptible staphylococci and against pneumococci, streptococci, gonococci, and corynebacteria; all are ineffective against Salmonella, *E. coli,* and other gram-negative coliform bacilli.

SYNCILLIN was more active against many of the test strains including some streptococci and staphylococci than either of its components. This demonstrates *in vitro* the phenomenon of isomeric complementarity.

TABLE 1

Minimum Concentrations of SYNCILLIN and Components Required to Inhibit a Wide Range of Bacteria



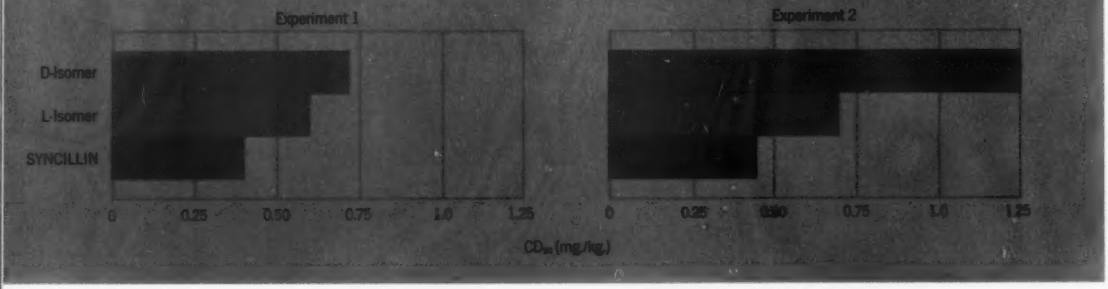
SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

ISOMERIC COMPLEMENTARITY CONFIRMED IN VIVO

To determine the median curative dose (CD_{50}) mice were infected with 100 times the lethal dose of *Staphylococcus aureus*. Each penicillin being tested was administered intramuscularly at the same time, and the dose required to cure half the animals determined. The greater effect of the mixture of the two isomers (SYNCILLIN) is shown in two independent experiments. (See Figure 1.) Note that isomeric complementarity is thus confirmed *in vivo*.

FIGURE 1 — Median Curative Dose (CD_m) for *Staphylococcus aureus* (var. Smith) Infections

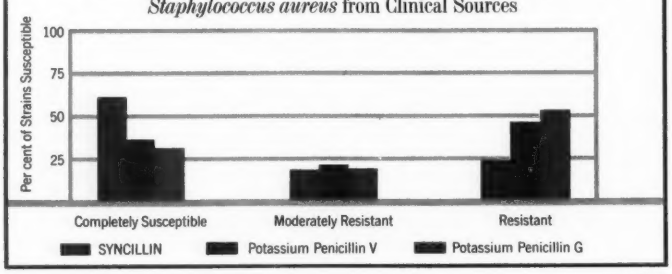


MANY STRAINS OF STAPHYLOCOCCI MORE SENSITIVE TO SYNCILLIN

SYNCILLIN has been tested against a large number of strains of *Staphylococcus aureus* isolated from clinical sources. Many organisms resistant to potassium penicillin G and potassium penicillin V proved sensitive to SYNCILLIN.

Wright[2] performed sensitivity studies on 54 strains, the majority of which were resistant or moderately resistant to penicillin V and penicillin G. Thirty-two (60%) of the strains were sensitive to SYNCILLIN, approximately twice as many as with the other penicillins. (See Figure 2.) In two-thirds of the isolates, SYNCILLIN produced inhibition at concentrations lower than those required for either of the other antibiotics. One strain was more sensitive to penicillin G.

FIGURE 2 – *In Vitro* Sensitivity of 54 Strains of Coagulase-Positive *Staphylococcus aureus* from Clinical Sources

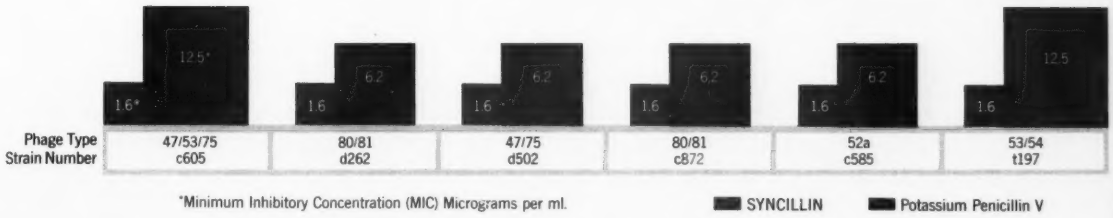


Adapted from Wright[2]

Of equal interest are the findings of White.[3] Six penicillin-resistant strains of staphylococci were isolated from hospital infections. None was sensitive to potassium penicillin V. All were sensitive to SYNCILLIN. (See Figure 3.)

FIGURE 3

Minimum Concentrations of SYNCILLIN Required to Inhibit
Hospital Strains of *Staphylococcus aureus* Resistant to Potassium Penicillin V

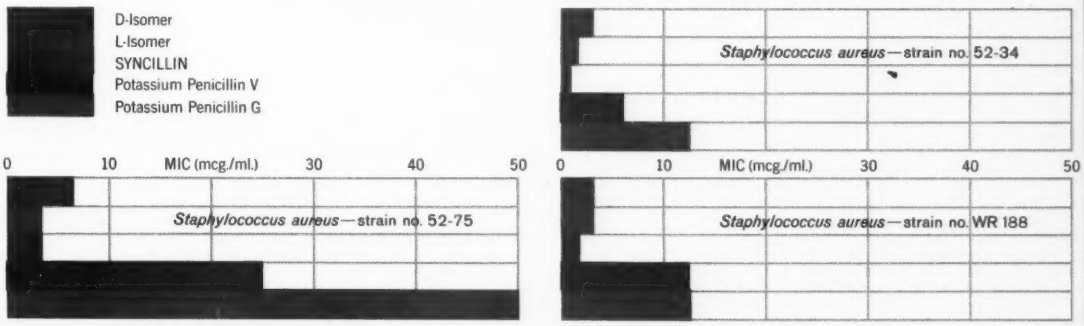


The efficacy of SYNCILLIN against the type 80/81 Staphylococcus (dangerous and widespread in hospitals) is worthy of special attention.

The complementary action of the component isomers is also seen with strains of staphylococci resistant to penicillins. Note that SYNCILLIN is more effective than either isomer against strains 52-34 and WR 188. (See Figure 4.) Against all three strains, SYNCILLIN is effective at concentrations below serum levels, while penicillins V and G are ineffective.

FIGURE 4

Minimum Inhibitory Concentrations (MIC) for Coagulase-Positive
Penicillin-Resistant Strains of *Staphylococcus aureus*



Isomeric complementarity has thus been demonstrated for:

— *certain penicillin-susceptible streptococci, staphylococci and corynebacteria* in vitro *(Table 1)*

— *penicillin-susceptible staphylococci* in vivo *(Figure 1)*

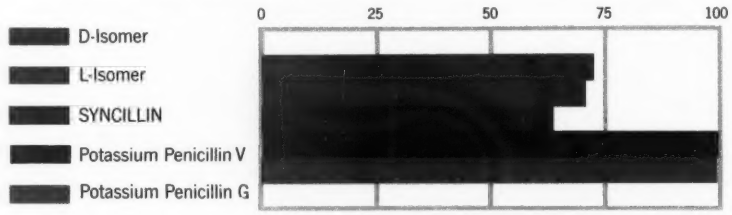
— *penicillin-resistant staphylococci* in vitro *(Figure 4)*

ISOMERIC COMPLEMENTARITY SHOWN BY REDUCED RATE OF INACTIVATION BY PENICILLINASE

Bacterial resistance to penicillin has been attributed to the action of penicillin-inactivating enzymes produced by the invading organisms.[4] As shown in Figure 5, SYNCILLIN is less affected by staphylococcal penicillinase than either of its component isomers – a further demonstration of isomeric complementarity. Further, SYNCILLIN is shown to be less inactivated by this enzyme than penicillin V and penicillin G.

Resistance to SYNCILLIN develops in a slow, step-wise manner characteristic of other penicillins, in contrast to the usually rapid development of resistance to streptomycin.

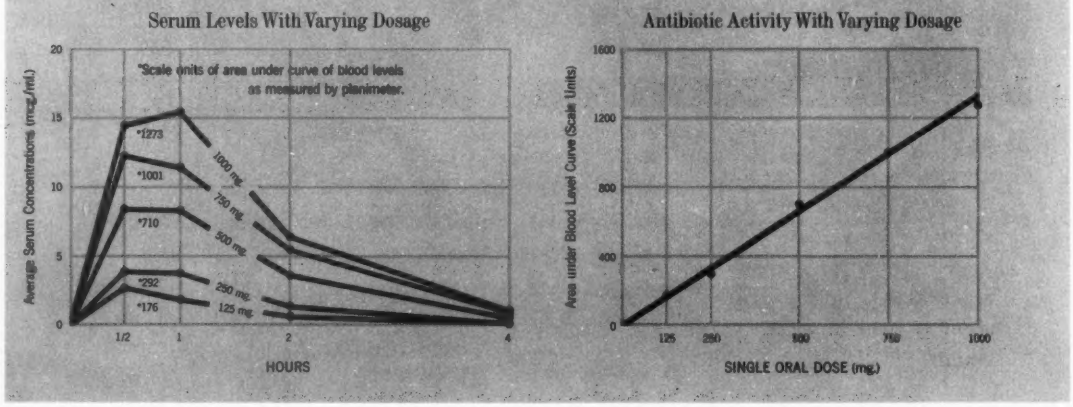
FIGURE 5—Effect of Staphylococcal Penicillinase on Different Penicillins



ANTIBIOTIC ACTIVITY DIRECTLY PROPORTIONAL TO ORAL DOSAGE

Cronk[5] studied blood levels after administering varying amounts of SYNCILLIN. (Figure 6.) Total antibiotic activity (obtained by measuring areas under curves with a planimeter) increases rapidly as the dose is doubled. These data show that increased dosage markedly increases serum concentration and thus may enhance the drug's effectiveness.

FIGURE 6



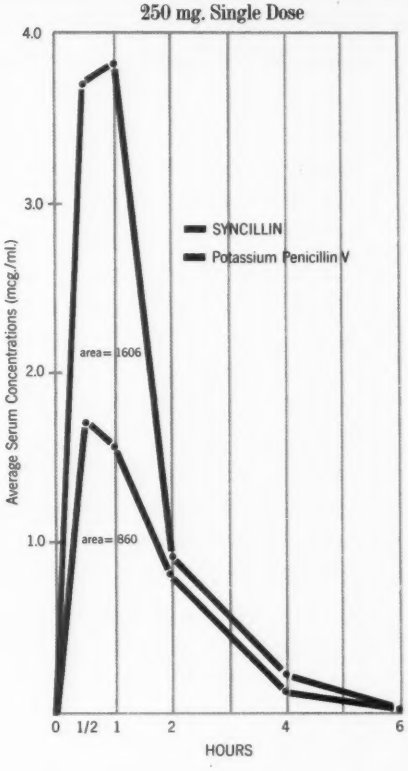
BLOOD LEVELS TWICE AS HIGH AS WITH POTASSIUM PENICILLIN V AFTER ORAL ADMINISTRATION

Wright[6] performed comparative crossover blood level studies on volunteer subjects receiving equivalent amounts of potassium penicillin V and SYNCILLIN. The peak concentrations attained during the first hour after administration were twice as high with SYNCILLIN.

The total antibiotic activity as measured by the area under the curves (see Figure 7) indicates an almost 2 to 1 superiority of SYNCILLIN (1606) over potassium penicillin V (860).

The higher blood levels may be of value with organisms of only moderate penicillin-sensitivity where doubling the blood concentration may be essential for effective bactericidal action. In addition these higher levels may be necessary where there is infection in areas with a poor blood supply.[7] Under these circumstances a higher blood concentration may provide the increased diffusion pressure required to deliver adequate amounts to the tissue.

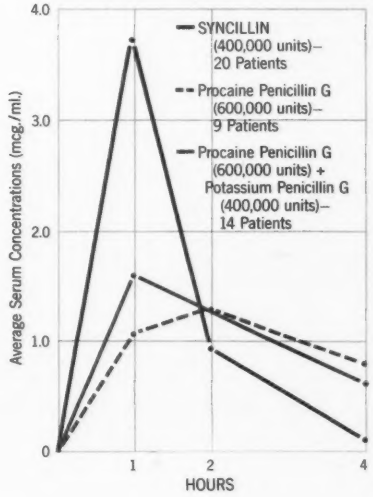
FIGURE 7
20 Subject Crossover
250 mg. Single Dose



BLOOD LEVELS MUCH HIGHER THAN WITH INTRAMUSCULAR PENICILLIN G

In addition, blood levels attained with oral SYNCILLIN[6] are much higher than those with intramuscular penicillin G.[8a, b] (See Figure 8.) Note that the level at one hour for SYNCILLIN (3.8 mcg./ml.) is more than twice as high as with procaine penicillin G, even when reinforced with potassium penicillin G (1.6 mcg./ml.). Since penicillins are *bactericidal,* these intermittent high serum levels can be clinically significant. Thus, SYNCILLIN offers the promise of superior efficacy via the safer oral route.

FIGURE 8—Serum Levels after Oral Administration of SYNCILLIN (250 mg.) and after Intramuscular Injection of Penicillin G



SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

REDUCED HAZARD OF SERIOUS ALLERGENICITY BY SAFER ORAL ROUTE

SYNCILLIN has been administered in multiple doses to 437 patients and volunteers. One patient developed itching during therapy, possibly an allergic side effect. Another had a purpuric rash, but no relationship to SYNCILLIN was established. No reactions were observed in 9 patients with a known history of sensitivity to penicillin.

While the above data suggests the possibility of reduced allergenic hazard, no definite conclusions may be drawn at this time. *The usual precautions for oral penicillin therapy should be observed.* Patients with histories of asthma, hay fever, urticaria, or previous penicillin-sensitivity should especially be watched carefully. Since SYNCILLIN is administered orally, it may be expected to be safer than parenteral penicillin.

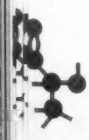
As Flippin[9] recently stated, ". . . it is well established that serious allergy to the drug [penicillin] is most likely to occur following parenteral administration, especially after repeated intramuscular injections; the oral route is least likely to initiate severe hypersensitivity reactions. This can be explained partly by the fact that when reactions develop following oral medication, they are usually slow enough to treat symptomatically; thus the progression of the reaction can usually be interrupted. . . . In view of the relatively high incidence of severe allergy to injectable penicillin, it would seem advisable to employ oral penicillin routinely, except in the control of infections involving the blood stream, endocardium, meninges, etc., in which cases the parenteral route remains the preferred treatment."

SYNCILLIN, like other penicillins, is essentially free of other toxicity. No hematopoietic, hepatic, or renal toxicity was observed in 210 volunteers receiving 1 gm. daily for 2 to 3 weeks.[10]

CLINICAL EFFICACY DEMONSTRATED IN PENICILLIN-SENSITIVE INFECTIONS

Clinical trials conducted by Blau and Kanof,[11] White,[12] Prigot,[13] Robinson,[14] Dube,[15] Ferguson,[16] Rutenburg,[17] Richardson,[18] Bunn,[19] Cronk,[5] Kligman,[10] and Yow [20] demonstrated the efficacy of SYNCILLIN in a variety of streptococcal, staphylococcal, pneumococcal, and gonococcal infections. Conditions treated included respiratory, skin, soft tissue, wound, and chronic urinary tract infections; acute gonorrhea; cellulitis; septicemia; otitis media; gingivitis; and Vincent's angina. In a few patients SYNCILLIN was used for rheumatic fever or gonorrheal prophylaxis.

One hundred seventy-two of one hundred ninety-six patients responded favorably to SYNCILLIN. The failures included 1 patient with pustular dermatoses, 10 elderly patients with chronic urinary tract infections, 1 patient with gonorrhea, 1 patient with a gram-negative infection, and 10 patients with staphylococcal infections. Lack of response of staphylococcal infections was attributed to the presence of resistant organisms or local suppurative foci requiring drainage.



Relatively few side effects were encountered. One patient experienced moderate itching of the skin which was controlled by an antihistamine. Another reported pruritus ani which did not interfere with therapy. Diarrhea occurred in 4 instances. There was one purpuric rash, but no relationship to SYNCILLIN could be established.

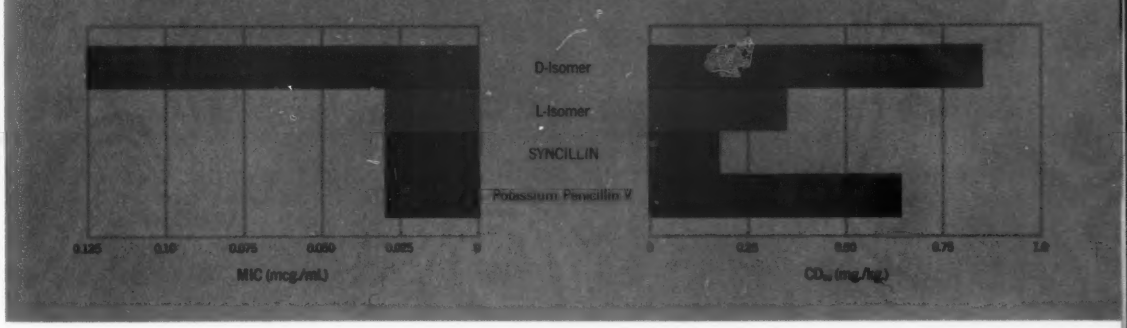
Clinical response usually begins within 24 hours in infections susceptible to SYNCILLIN. Recovery occurs in 4 to 7 days depending upon the severity of the infection. Gonorrheal infections respond very promptly to SYNCILLIN; 500 mg. b.i.d. for two days usually produce bacteriologic cures.

IMPROVED ANTIBIOTIC EFFECT FROM COMPLEMENTARY ACTION OF ISOMERS

SYNCILLIN is a mixture of isomers. The L-isomer is 2 to 17 times more active than the D-isomer against many of the organisms tested. Furthermore, the D- and L-isomers have other distinguishing chemical, pharmacological, and microbiological properties. Their *in vivo* and *in vitro* activities differ for many important pathogens. *Against many of the organisms tested, the combination of isomers* (SYNCILLIN) *is much more active than the stronger isomer alone.* This phenomenon of isomeric complementarity is not always demonstrable, for in a few instances SYNCILLIN is slightly less active.

Isomeric complementarity has previously been demonstrated *in vitro* (Figure 4) and *in vivo* (Figure 1). Figure 9 reveals a third form of superiority related to isomeric complementarity. Equal concentrations of SYNCILLIN and penicillin V were required to inhibit this growth of staphylococci *in vitro.* But, *in vivo,* a much smaller amount of SYNCILLIN *(one-third that of penicillin V)* was effective in an experimental infection with the same strain. These observations on complementary action indicated the advantage of producing the mixture of isomers as the medication to be made available for clinical therapy.

FIGURE 9—Comparison of CD_m and MIC Values Against *Staphylococcus aureus* (var. Smith)



Isomeric complementarity has thus been demonstrated for:

—*certain penicillin-susceptible streptococci, staphylococci and corynebacteria* in vitro *(Table 1)*

—*penicillin-susceptible staphylococci* in vivo *(Figures 1 and 9)*

—*penicillin-resistant staphylococci* in vitro *(Figure 4)*

—*staphylococcal penicillinase antibiotic inactivation (Figure 5)*

SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

Indications:

SYNCILLIN is recommended in the treatment of infections caused by pneumococci, streptococci, gonococci, corynebacteria, and penicillin-sensitive staphylococci. In addition, SYNCILLIN is effective against certain strains of staphylococci resistant to other penicillins.

SYNCILLIN, like other oral penicillins, is not recommended at the present time in deep-seated or chronic infections, subacute bacterial endocarditis, meningitis, or syphilis.

Dosage:

125 mg. or 250 mg. three times daily, depending on the severity of infection. Larger doses (e.g., 500 mg. t.i.d.) may be used for more severe infections. SYNCILLIN may be administered without regard to meals.

Beta hemolytic streptococcal infections should be treated with SYNCILLIN for at least ten days.

Precautions:

While present data suggest the possibility of reduced allergenic hazard, no definite conclusions may be drawn at this time. *Therefore the usual precautions with oral penicillin therapy must be observed.* Patients with histories of asthma, hay fever, urticaria, or previous reactions to penicillin should be watched with special care.

Diarrhea has been reported occasionally following heavy dosage. If this occurs, the interval between dosages should be lengthened.

If superinfection occurs during therapy, appropriate measures should be taken.

Since some strains of staphylococci are resistant to SYNCILLIN as well as to other penicillins, cultures and sensitivity tests should be performed where indicated by clinical judgment. As is true with all antibiotics, clinical response does not always correlate with laboratory bacterial sensitivity reports.

Supply:

125 and 250 mg. tablets, bottles of 25 and 100. 125 mg. powder for oral solution, 60 ml. vials.

References: 1. Lein, J.: Microbiology report to Bristol Laboratories Inc. 2. Wright, W. W.: Microbiology report to Bristol Laboratories Inc. 3. White, A. C.: Microbiology report to Bristol Laboratories Inc. 4. Dubos, R. J.: Bacterial and Mycotic Infections of Man, 3rd edition, Philadelphia, J. B. Lippincott Co., p. 690. 5. Cronk, G. A.: Clinical report to Bristol Laboratories Inc. 6. Wright, W. W.: Clinical report to Bristol Laboratories Inc. 7. Kass, E. H.: Am. J. Med. *18*:764 (May) 1955. 8a. White, A. C.; Couch, R. A.; Foster, F.; Calloway, J.; Hunter, W., and Knight, V.: in Welch, H. and Marti-Ibañez, F.: Antibiotics Annual — 1955-1956, Medical Encyclopedia, Inc., New York, 1956, p. 490. b. Data on file — at Bristol Laboratories. 9. Flippin, H. F.: Pennsylvania M. J. *62*:864 (June) 1959. 10. Kligman, A.: Clinical report to Bristol Laboratories Inc. 11. Blau, S., and Kanof, N.: Clinical report to Bristol Laboratories Inc. 12. White, A. C.: Clinical report to Bristol Laboratories Inc. 13. Prigot, A.: Clinical report to Bristol Laboratories Inc. 14. Robinson, C.: Clinical report to Bristol Laboratories Inc. 15. Dube, A. H.: Clinical report to Bristol Laboratories Inc. 16. Ferguson, B.: Clinical report to Bristol Laboratories Inc. 17. Rutenburg, A. M.: Clinical report to Bristol Laboratories Inc. 18. Richardson, J. H.: Clinical report to Bristol Laboratories Inc. 19. Bunn, P. A.: Clinical report to Bristol Laboratories Inc. 20. Yow, E. M.: Clinical report to Bristol Laboratories Inc.

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NIAMID*
brightens life for the aged

NIAMID gives the depressed elderly person a new sense of well-being. The family will notice a sunnier outlook, an alert interest in group activities, a renewed awareness of personal appearance, and a return of appetite. Your patient will be more cooperative and less demanding.

You can expect to see the same excellent response to NIAMID in a wide variety of depressive syndromes—acute or chronic, mild or severe, whether associated with long-standing or incurable illness, or masquerading as organic disease.

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DOSAGE: Start with 75 mg. daily in single or divided doses, and adjust according to patient response. NIAMID acts slowly, without rapid jarring of physical or mental processes. Some patients respond to NIAMID within a few days, but for full therapeutic benefit, most require at least two weeks. NIAMID is available as 25 mg. (pink) and 100 mg. (orange) scored tablets.

Already clinically proved in several thousand patients—

Complete references and a Professional Information Booklet giving detailed information on NIAMID *are available on request from the Medical Department, Pfizer Laboratories, Division, Chas. Pfizer & Co., Inc., Brooklyn 6, N. Y.*

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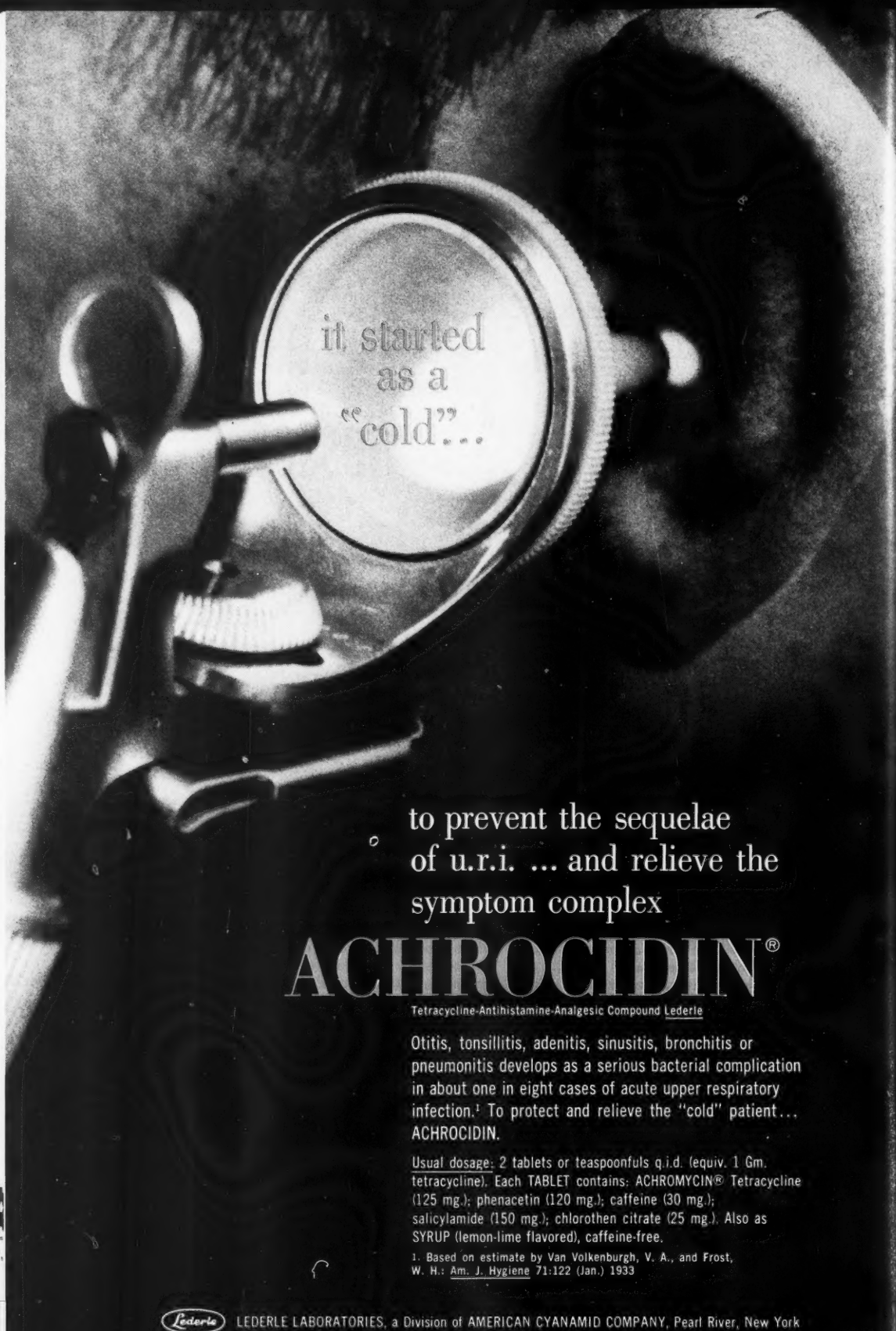

to prevent the sequelae of u.r.i. ... and relieve the symptom complex

ACHROCIDIN®

Tetracycline-Antihistamine-Analgesic Compound Lederle

Otitis, tonsillitis, adenitis, sinusitis, bronchitis or pneumonitis develops as a serious bacterial complication in about one in eight cases of acute upper respiratory infection.[1] To protect and relieve the "cold" patient... ACHROCIDIN.

Usual dosage: 2 tablets or teaspoonfuls q.i.d. (equiv. 1 Gm. tetracycline). Each TABLET contains: ACHROMYCIN® Tetracycline (125 mg.); phenacetin (120 mg.); caffeine (30 mg.); salicylamide (150 mg.); chlorothen citrate (25 mg.). Also as SYRUP (lemon-lime flavored), caffeine-free.

1. Based on estimate by Van Volkenburgh, V. A., and Frost, W. H.: Am. J. Hygiene 71:122 (Jan.) 1933

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Tetracycline-Triple Sulfa Combination (TETREX® $\overline{c}$ T/S) in the Treatment of INFECTION

It is generally agreed that it is ideal to withhold antibiotic and chemotherapeutic drugs until after sensitivity tests show which antibacterial agent will be most effective. But very often, in actual practice, the physician knows that delay in starting antibacterial treatment may be detrimental to the welfare of his patient. He must then select the therapy to meet the most serious and immediate threats to the patient.

Why Combination Therapy?

Certain infections do not respond as well to a single agent as to a combination. *Hemophilus influenzae* infections, which are frequent in children, are a particularly serious threat to infants and children up to about 3 or 4 years of age since they have not yet built up any appreciable immunity. Serious complications such as influenzal pneumonia, empyema, or meningitis may develop, especially in this age group. In fact, except for those periods when meningococcal meningitis is epidemic, *H. influenzae* is the most frequent cause of meningitis.[1] This gram-negative organism is highly susceptible both to the tetracyclines and to the sulfonamides. Even in severe infections, therapeutic failure can be virtually eliminated by giving sulfonamides plus tetracycline.[1] These two agents together constitute the treatment of choice, and give better results than either alone.[2]

Sulfonamides remain the drugs of choice for all meningococcal infections, including meningitis. They readily penetrate the blood-brain barrier and pass into the cerebrospinal fluid in good concentrations.[3] In treating overwhelming meningococcal infections, and complicating infections of the upper respiratory tract caused by other organisms, the addition of tetracycline to sulfas can be valuable.[4]

In recent years the sulfonamides have again been prescribed more and more frequently. In certain serious infections, better results can be obtained with a combination of antibiotic and sulfonamide than with either drug alone (e.g., severe pneumococcal pneumonia or pneumococcal meningitis[5]). Furthermore, mixed infections, to which young children are particularly susceptible, often respond only to combination therapy such as tetracycline with sulfonamides (TETREX $\overline{c}$ T/S).

Why Triple Sulfas?

Some sulfonamides, though therapeutically useful, frequently crystallize and cause renal damage. Sulfonamide mixtures are designed to prevent this effect. It is known that different substances can coexist in solution without interfering with each other's solubility. In such a solution each component behaves as if it alone were present. Thus, a much larger total amount of sulfonamide can exist in the urine without precipitating if a mixture is administered than if the same amount of only one compound is given.

Similarly, there is less danger of hypersensitivity with mixtures. The incidence of sensitization varies directly with the dosage and is limited to the particular sulfa given. Simultaneous use of several sulfa compounds, each in partial dosage, tends to keep each drug below its own sensitization level.[3] As with all sulfonamides, it is advisable to check for possible blood dyscrasias, rash, or renal toxicity during extended administration.

TETREX $\overline{c}$ T/S, by combining only 167 mg. each of sulfadiazine, sulfamerazine, and sulfamethazine, practically eliminates serious renal damage and sensitization reactions due to sulfonamides while retaining the therapeutic efficacy of the total dose.

TETREX $\overline{c}$ T/S can be administered with confidence in all severe and mixed infections due to tetracycline-sensitive and sulfonamide-sensitive organisms, including infections of the upper respiratory, urinary, and gastrointestinal tracts.

References: 1. Alexander, H. E.: The hemophilus group. In: Dubois, R. J.: Bacterial and Mycotic Infections of Man. Ed. 3, Philadelphia, J. B. Lippincott Co., 1958, p. 470ff. 2. Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics. Ed. 2, New York, The Macmillan Co., 1956, pp. 1322-1323. 3. Beckman, H.: Drugs — Their Nature, Action, and Use. Philadelphia, W. B. Saunders Co., 1958, pp. 527-528. 4. Dingle, J. H.: Meningococcal infections. In: Cecil, R. L., and Loeb, R. F.: A Textbook of Medicine. Ed. 9, Philadelphia, W. B. Saunders Co., 1955, p. 196ff. 5. Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics. Ed. 2, New York, The Macmillan Co., 1956, p. 1308.

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relief comes fast and comfortably

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...a new way to relieve pain and stiffness in muscles and joints

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"TIGHT NECK"

TRAUMATIC STRAINS AND BRUISES

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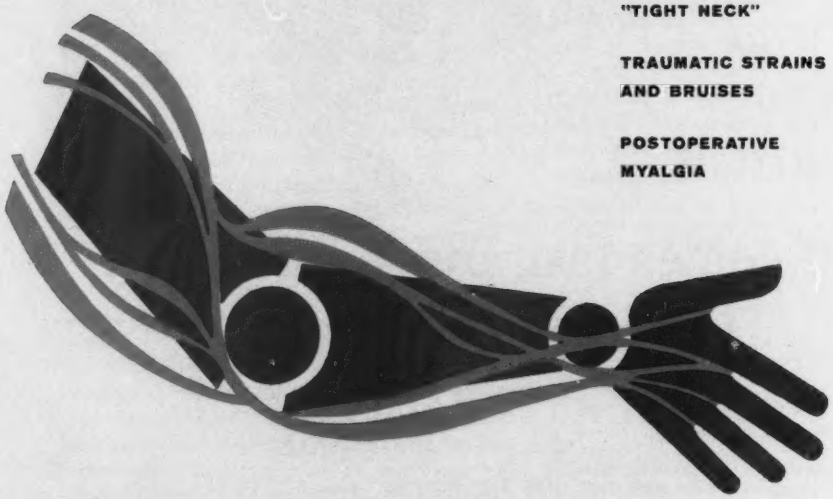

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Many women don't know that a vinegar douche is as old-fashioned as the copper tub, a relic of an empiric age.[1] Acids actually make mucus discharge more tenacious. On the other hand, soaps and harsh alkali are irritating. A detergent douche – TRICHOTINE, the only major douche containing sodium lauryl sulfate – is the modern, more efficient yet gentler vaginal irrigant.

The detergent action of TRICHOTINE assures greater penetration of viscid mucus, better dispersion of the healing medicaments on the mucosal surface, and more efficient removal of vaginal discharge.

If there is any doubt in your mind, compare TRICHOTINE with vinegar or any other

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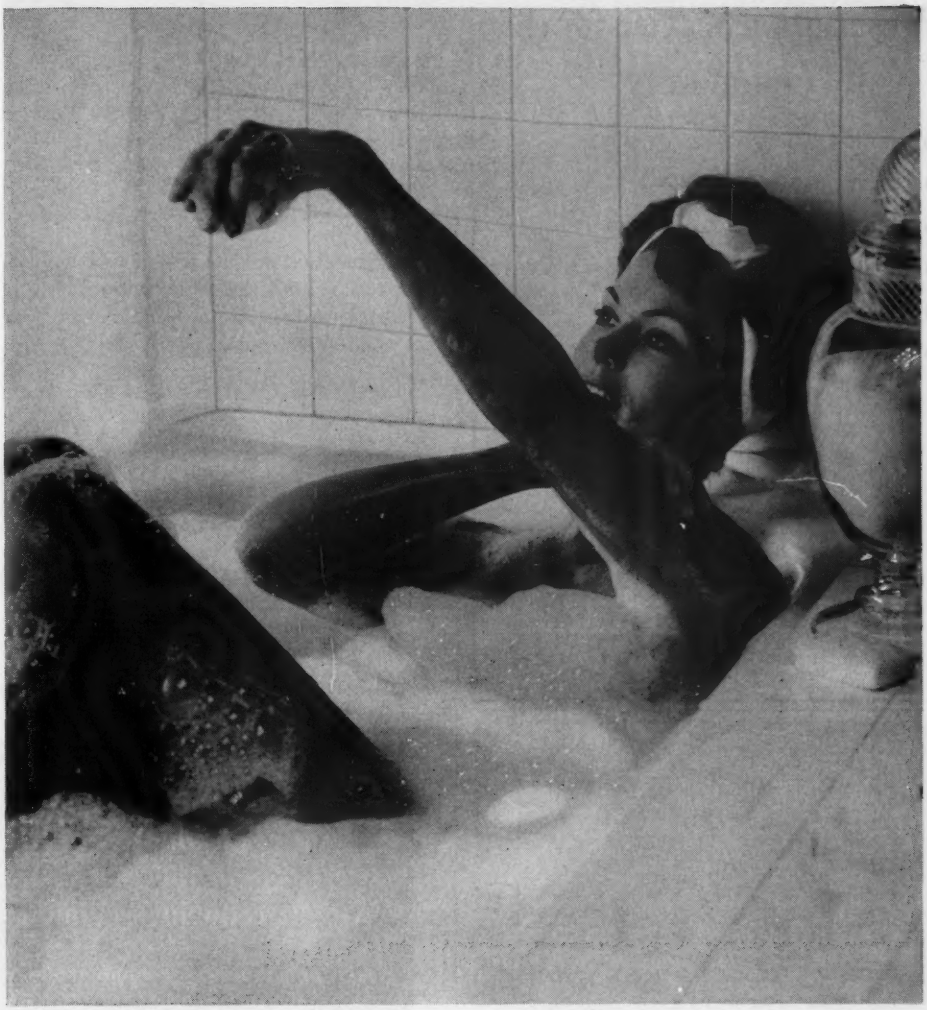

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The pH changes produced by any low pH douche last only a few minutes[2] and are of questionable value in healing.[3] TRICHOTINE actually favors epithelial growth and healing,[3] assures maximum cleansing, soothes inflamed mucus membranes.

TRICHOTINE is indicated in the management and treatment of cervicovaginitis and leukorrheas, alone or in conjunction with other antimicrobials. TRICHOTINE is ideal for routine feminine hygiene – safe, gentle and effective.

2. Karnaky, K.J.: J.A.M.A. 157:1155, 1955 (August)
3. Scheinberg et al: Surgery 24:972, 1948 (Dec.).

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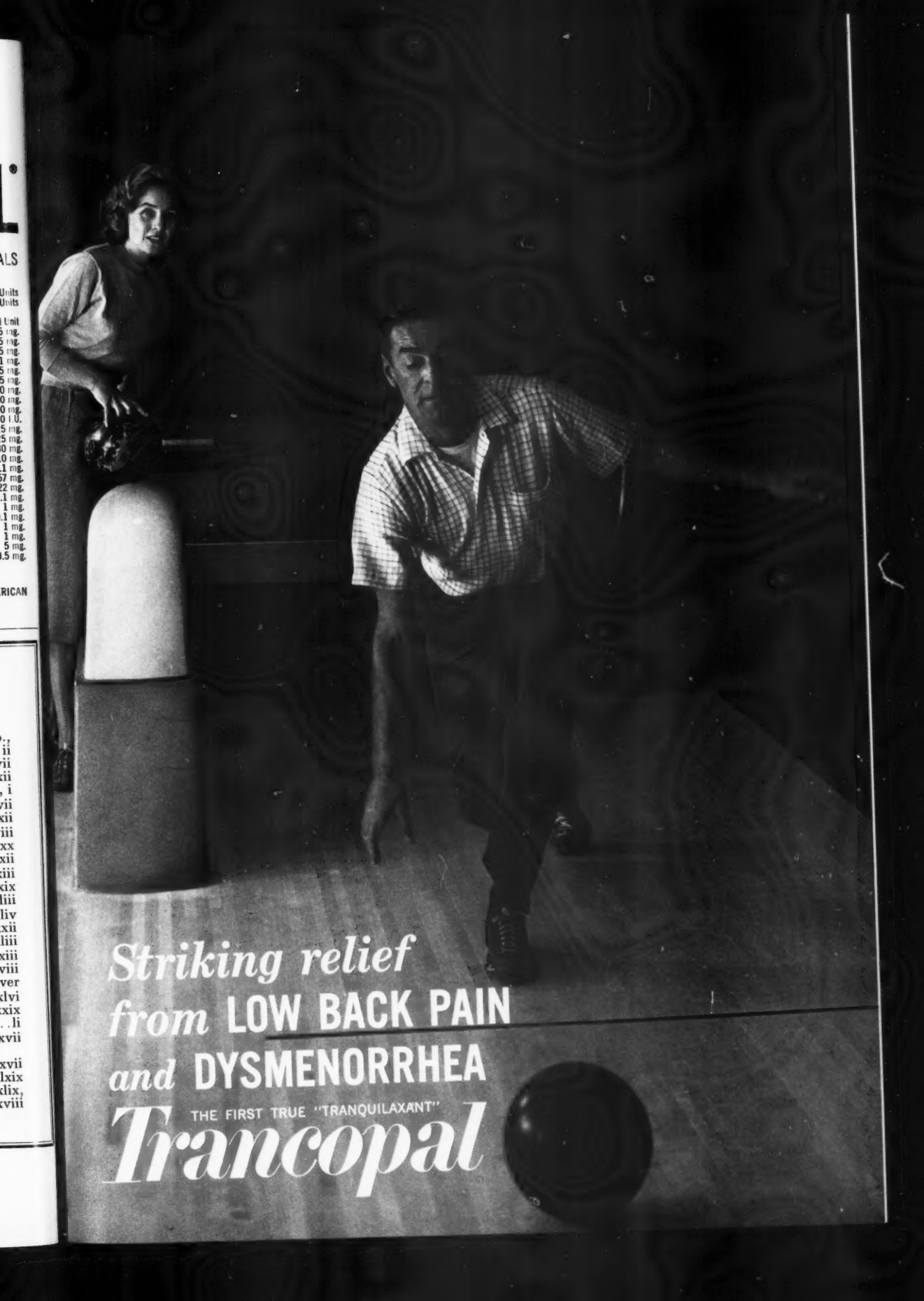
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and DYSMENORRHEA
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Case Profile*

A 28-year-old married woman, a secretary in a booking agency, complained of severe and consistent pain and cramps in the abdomen during her menstrual periods. Psychologically, she described the first two days as "climbing the walls." Menarche occurred at age 13. She has a regular twenty-eight day menstrual cycle and a four day menstrual period.

Trancopal was given in a dose of 100 mg. four times a day for the first two days of the four day period. In addition to the relief of the dysmenorrhea she also noticed disappearance of a "bloated feeling" that had previously annoyed her. She has now been treated with Trancopal for one and one-half years with excellent results. Other medication, such as codeine or aspirin with codeine, had relieved the pain, but the patient had had to stay home. Because her father is a physician, many commercial preparations had been tried prior to Trancopal, but no success had been achieved.

Before taking Trancopal this patient missed one day of work every month. For the past year and a half she has not missed a day because of dysmenorrhea.

for dysmenorrhea
and premenstrual tension

THE FIRST TRUE "TRANQUILAXANT"

Trancopal®

for low back pain

Case Profile*

A 42-year-old truck driver and mover injured his back while moving a piano. The pain radiated from the sacral region down to the region of the Achilles tendon on the right side. X-rays for ruptured disc revealed nothing pertinent. The day of the injury he was given Trancopal immediately after the physical examination. Although 100 to 200 mg. three times a day were prescribed, the patient on his own responsibility increased the dosage of Trancopal to 400 mg. three times a day. This dosage was continued for three days and then gradually reduced over a ten day period. During this time, the patient continued to drive his truck. The muscle spasm was completely controlled and no apparent side effects were noted.

For the past six months, the patient has continued to take Trancopal 100 to 200 mg. as needed for muscle spasm, particularly during strenuous days.

**Clinical Reports on file at the Department of Medical Research, Winthrop Laboratories.*

Turn page for complete listings of Indications and Dosage.

THE FIRST TRUE "TRANQUILAXANT"

Trancopal

potent MUSCLE RELAXANT

effective TRANQUILIZER

- In musculoskeletal disorders, effective in 91 per cent of patients.[1]
- In anxiety and tension states, effective in 89 per cent of patients.[1]
- Low incidence of side effects (2.3 per cent of patients). Blood pressure, pulse rate, respiration and digestive processes are unaffected by therapeutic dosage. It does not affect the hematopoietic system or liver and kidney function.
- No gastric irritation. Can be taken before meals.
- No clouding of consciousness, no euphoria or depression.

Indications [1-6]

Musculoskeletal:

- Low back pain (lumbago, etc.)
- Neck pain (torticollis)
- Bursitis
- Rheumatoid arthritis
- Osteoarthritis
- Disc syndrome
- Fibrositis
- Ankle sprain, tennis elbow
- Myositis
- Postoperative muscle spasm

Psychogenic:

- Anxiety and tension states
- Dysmenorrhea
- Premenstrual tension
- Asthma
- Angina pectoris
- Alcoholism

Now available in two strengths:

Trancopal Caplets®,
100 mg. (peach colored, scored), bottles of 100.

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Trancopal Caplets,
200 mg. (green colored, scored), bottles of 100.

Dosage: Adults, 100 or 200 mg. orally three or four times daily. Relief of symptoms occurs in from fifteen to thirty minutes and lasts from four to six hours.

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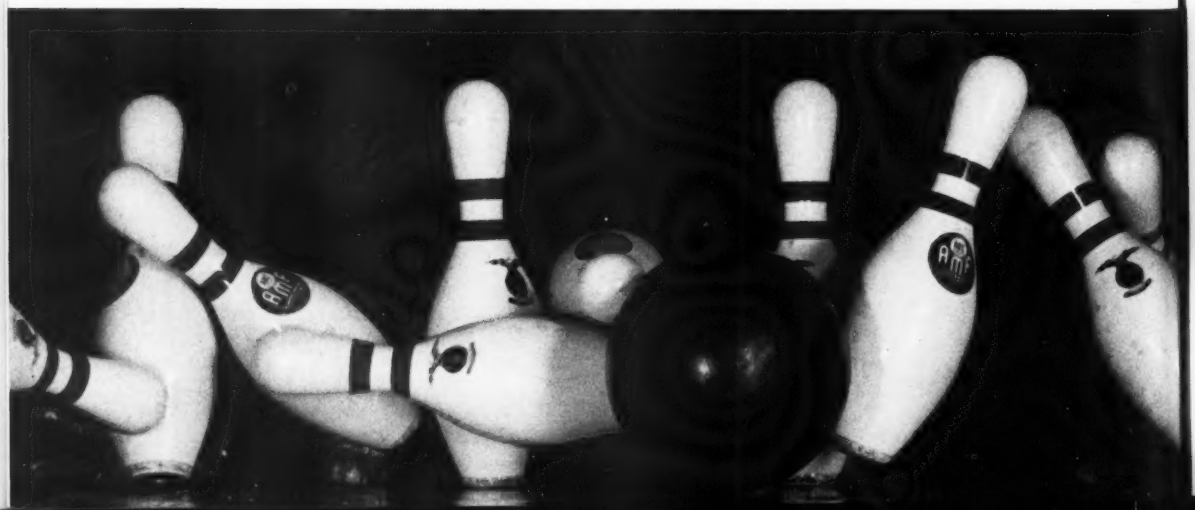
New York 18, N. Y.

References: 1. Collective Study, Department of Medical Research, Winthrop Laboratories. 2. Lichtman, A. L.: New developments in muscle relaxant therapy, *Kentucky Acad. Gen. Pract. J.* 4:28, Oct., 1958. 3. Lichtman, A. L.: Relief of muscle spasm with a new central muscle relaxant, chlormezanone (Trancopal), Scientific Exhibit, Meeting of the International College of Surgeons, Miami Beach, Fla., Jan. 4-7, 1959. 4. Ganz, S. E.: Clinical evaluation of a new muscle relaxant (chlormethazanone), *J. Indiana M. A.* 52:1134, July, 1959. 5. Mullin, W. G., and Epifano, Leonard: Chlormezanone, a tranquilizing agent with potent skeletal muscle relaxant properties, *Am. Pract. Digest Treat.* 10:1743, Oct., 1959. 6. Shanaphy, J. F.: Chlormezanone (Trancopal) in the treatment of dysmenorrhea; a preliminary report, *Current Therap. Res.* 1:59, Oct., 1959.



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